



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : BORODY *et al.*

Art Unit : 1616

Serial No. : 10/506,728

Examiner : Holt, Andriae M.

Filed : June 27, 2005

Confirm. No.: 7029

Title : **ELECTROLYTE PURGATIVE**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

ATTACHMENTS

1. DECLARATION of Dr. Thomas J. Borody Pursuant to 37 C.F.R. § 1.132
2. CLINICAL STUDY REPORT entitled "A Phase II, Comparative, Single-blinded, Randomised Study to Evaluate the Efficacy and Safety of Hypertonic Solution Combined with PicoPrep[™] Capsules Compared to PicoPrep[™] Capsules Alone, Standard Glycoprep[™] and Standard PicoPrep[™] as a Bowel Preparation" (30 June 2006)
3. Calculation of amount of sodium salt and sugar in the compositions of Kawakami.
4. The Merck Index, 9th ed. (1976), entry **8343**, page 1111.
5. Hoy *et al.*, Drugs 69(1): 123-136 (2009).



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DECLARATION PURSUANT TO 37 C.F.R. §1.132

Sir:

I, **Thomas J. Borody**, declare as follows,

1) I am an inventor of the above-captioned application, which is the National Stage of International Application. No. PCT/AU03/00257, filed March 4, 2003, which claims benefit of priority to Australian provisional patent application Serial No. PS 0887, filed March 4, 2002.

2) I am a Gastroenterologist. I obtained my BSc and MBBS from the University of New South Wales. I obtained my Ph.D. in medicine from the University of Newcastle and my M.D. from the University of New South Wales. I have been a Fellow of the Royal Australasian College of Physicians since 1982. I have been a Fellow of the American College of Gastroenterology since 1993 and a Fellow of the American College of Physicians (Philadelphia, PA) since 2002. I was a Clinical Fellow in Gastroenterology at the Mayo Clinic in Rochester, Minnesota. I am the Founder and have been the Medical Director for the Centre for Digestive Diseases in New South Wales since 1985 and have been a Consulting Gastroenterologist to the Sydney Adventist Hospital since 1995.

3) I have published more than 120 scientific articles. I am a reviewer for the Medical Journal of Australia, the American Journal of Gastroenterology, Digestive Diseases and Sciences and the Journal of Gastroenterology and Hepatology. I am an inventor on 18 issued US patents.

4) I have reviewed the Office Action, mailed February 26, 2009, in connection with the above-captioned application.

5) The above-captioned application provides compositions that can be used for orthostatic lavage to clean the bowel of fecal matter, as a simple purgative or in electrolyte replacement therapy. The pending claims recite compositions for use in a purgative and methods of inducing purgation of the colon of a patient.

6) The Office Action cites the combination of Kawakami (JP 05306221) and Colliopoulos (U.S. Pat. No. 5,232,699) and Cockerill (U.S. Pat. No. 4,452,779) in the rejection of certain of the claims. Kawakami describes isotonic purgative preparations for irrigation of the intestines. Colliopoulos describes laxatives containing psyllium and sennoside, such as in the form of a baked wafer. Laxative compositions containing senna or sennosides are known to have undesirable side effects, such as pain, bloating and cramping. Cockerill describes diuretic compositions and methods for removing excess fluid from mammary tissue of a lactating mammal in order to improve the quality and quantity of milk from the mammary tissue without dehydrating the mammal. There is no mention in Cockerill that its composition could be used as a purgative to cleanse the colon. The compositions are in the form of a powder that is dispersed on dry feed.

7) The composition of the instant claims can be used in a purgative, such as a hypertonic purgative. As described in the specification, a purgative including the instant composition is more effective as a bowel cleansing preparation than existing purgative agents. The various salts and the xylose or other minimally degradable sugar in the instant compositions are used to increase the tonicity of the active solution. When prepared as a hypertonic solution, a reduced volume of the active agent can be consumed, resulting in better tolerability and reduction in adverse side effects, thereby improving patient compliance. The addition of short chain minimally degradable carbohydrates in the instant composition avoids the gas formation, bloating and cramps that can be caused by degradable sugars used in commercial products. The salts reduce the electrolyte loss during bowel purgation. In the instant compositions, palatable salts such as gluconate, citrate and aspartate are used to improve palatability since these salts are known to locally reduce stimulation of salt receptors found on the tongue.

8) A clinical study, entitled "A Phase II, Comparative, Single-blinded, Randomised Study to Evaluate the Efficacy and Safety of Hypertonic Solution Combined with PicoPrep™ Capsules Compared with PicoPrep™ Capsules Alone, Standard Glycoprep™ and Standard PicoPrep™ as Bowel Preparation," was undertaken to compare a hypertonic solution including the composition claimed in the instant application to commercially available bowel cleansers, such as Glycoprep™ and PicoPrep™.

9) Glycoprep™ is a PEG-based purgative containing PEG 3350, sodium chloride, potassium chloride, sodium sulfate, ascorbic acid, aspartame and citric acid and is isotonic with respect to bowel content. Generally 3 liters of Glycoprep™ are administered.

10) PicoPrep™ is a magnesium citrate-based purgative. PicoPrep™ includes sodium picosulfate (a stimulant laxative), magnesium oxide, citric acid and aspartame. When dissolved in water, the magnesium oxide and citric acid components form magnesium citrate, an osmotic purgative. PicoPrep™ generally is administered as a 250 mL aqueous solution, followed by the administration of several glasses of water over the course of several hours.

11) The composition of Kawakami is an isotonic magnesium citrate solution that includes sodium chloride, potassium hydroxide and a degradable sugar such as sucrose. Thus, the composition of Kawakami is a magnesium citrate-based purgative similar in composition to PicoPrep™. It differs from PicoPrep™ in that it includes an easily digestible sugar and does not include sodium picosulfate. PicoPrep™ also is a more hypertonic solution. The composition of Kawakami is administered as a 900 mL aqueous solution.

12) The results of the clinical study are shown in the attached "Clinical Study Report." As can be seen from the results of the clinical study, purgatives that include the composition claimed in the instant application were found to be more effective at cleansing the bowel than standard magnesium citrate-based purgatives like PicoPrep™ preparations or PEG-based purgatives such as Glycoprep™ alone. In particular, purgatives that include the composition claimed in the instant application were rated significantly more effective in cleansing the transverse colon than standard magnesium citrate-based purgatives like PicoPrep™ preparations.

13) Because the composition described in Kawakami is a magnesium citrate-based purgative similar to PicoPrep™, and formulations that include the composition claimed in the instant application were found to be more effective at cleansing the bowel than a magnesium citrate-based purgative like PicoPrep™, it is expected that formulations that include the composition claimed in the instant application also would be more effective at cleansing the bowel than the magnesium citrate-based purgative described in Kawakami.

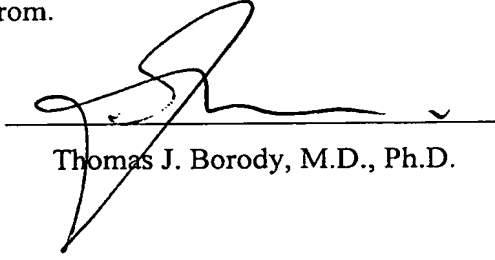
Applicant : BORODY *et al.*
Serial No. : 10/506,728
Filed : June 27, 2005

Attorney's Docket No.: 119381-00002 / 3703US
Declaration of Dr. Borody

14) I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Date

11/06/2009



Thomas J. Borody, M.D., Ph.D.

**“A Phase II, Comparative, Single-blinded, Randomised Study
to Evaluate the Efficacy and Safety of Hypertonic Solution
Combined with PicoPrep™ Capsules Compared with
PicoPrep™ Capsules Alone, Standard Glycoprep™ and
Standard PicoPrep™ as a Bowel Preparation.”**

Study No.: CDD02/C01

Clinical Study Report

Version 1 (30 June, 2006)

Investigational Product: Hypertonic solution and PicoPrep™ capsules
Indication Studied: Bowel preparation prior to colonoscopy
Design: Single blind, Randomised, Comparative

Study Initiation Date: 9th April 2003
Study Completion Date: 5th May 2004

Sponsor: Centre for Digestive Diseases
144 Great North Road
Five Dock, NSW
Australia, 2046

Investigator Site: Centre for Digestive Diseases
144 Great North Road
Five Dock, NSW
Australia, 2046

Principal Investigator: Prof Thomas Borody
Co-Investigators: Dr Antony Wettstein
Dr Sanjay Ramrakha
Dr John Saxon
Study Manager: Ms Rosa Surace
Study Co-ordinator: Ms Raquel Llorente

Archiving: The Centre for Digestive Diseases is responsible for the archiving of all essential study documentation for the total of 15 years from the date of completion above.

Note: This study was performed in compliance with Good Clinical Practices (GCP) TGA July 2002.

SIGNATURE / APPROVAL PAGE

Study Title: "A Phase II, Comparative, Single-blinded, Randomised Study to Evaluate the Efficacy and Safety of Hypertonic Solution Combined With PicoPrep™ Capsules Compared With PicoPrep™ Capsules alone, Standard Glycoprep™, and Standard PicoPrep™ as a Bowel Preparation."

Study Author(s): Prof Thomas Borody (Principal Investigator), Raquel Llorente (Study Co-ordinator) and Rosa Surace (Study Manager) from the Centre for Digestive Diseases Pty Ltd.

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Investigator: _____

Signature: _____

Affiliation: Study Site and Australian Sponsor

Date: _____

SYNOPSIS

| | | |
|--|--|---|
| Name of Sponsor: Centre for Digestive Diseases | Name of Finished Product: Hypertonic Solution | Name of Active Ingredients: Sodium Picosulfate, Xylose, Magnesium Sulfate, Sodium Chloride, Sodium Citrate, Potassium Glutamate, Chicken Flavouring |
| Title of Study: "A phase II, comparative, single-blinded, randomised study to evaluate the efficacy and safety of Hypertonic solution combined with PicoPrep™ capsules compared with PicoPrep™ capsules alone, standard Glycoprep™, and standard PicoPrep™ as a bowel preparation." | | |
| Investigators: Principal Investigator: Prof Thomas Borody Co-Investigators: Dr Antony Wettstein, Dr Sanjay Ramrakha, Dr John Saxon | | |
| Study Centre: Centre for Digestive Diseases, 144 Great North Road, Five Dock, NSW, 2046, AUSTRALIA | | |
| Study Period: 2nd quarter 2003 to 2nd quarter 2003 | Phase of Development: Phase II, therapeutic exploratory | |
| Objectives: <i>Primary Objective</i> - To evaluate the efficacy and safety of Hypertonic solution combined with PicoPrep™ capsules compared with PicoPrep™ capsules alone, standard Glycoprep™, and standard PicoPrep™ as a bowel preparation. <i>Secondary Objective</i> - To assess the side effects and compliance of the Hypertonic solution combined with PicoPrep™ capsules compared with PicoPrep™ capsules alone, and those of standard Glycoprep™, and standard PicoPrep™. | | |
| Methodology: A comparative study which compared the efficacy and safety of a new bowel preparation with currently marketed bowel preparations. Patient ratings were used to assess differences in tolerance and compliance. Doctor and Sedationist ratings were used to determine differences in efficacy between the bowel preparations. Adverse events were assessed to determine safety of bowel preparations. | | |
| Number of Subjects (planned and analysed): It was planned that 60 subjects were to fully complete the study (15 per arm). Sixty two subjects enrolled, with 59 subjects completing the study as per protocol. Due to subject withdrawals and randomisation the subject disposition was 15 subjects in Arm 1, 16 subjects in Arm 2, and 14 subjects in each of Arms 3 and 4. | | |
| Diagnosis and Main Criteria for Inclusion: Male and female subjects aged 18 to 70 years undergoing colonoscopy and with no other major concomitant illness that may interfere with subject's ability to enter the trial. | | |
| Test Product, Dose, Mode of Administration and Batch Number: Hypertonic solution and PicoPrep™ capsules. 25.015g Hypertonic solution in 350ml water plus 10 PicoPrep™ capsules at 3pm. 10 PicoPrep™ capsules at 6pm. Taken orally. Hypertonic solution batch no.: C0804. PicoPrep™ capsule batch no.: B0136N B11181. | | |
| Duration of Treatment: 1 day | Concomitant Medication Specified in Protocol: Diuretics, Indapamine, Carbamazepine, Lithium Carbonate, SSRIs and ACE inhibitors. | |
| Criteria for Evaluation: <i>Efficacy data included</i> – Patient, Doctor and Sedationist evaluation forms. <i>Safety data included</i> – urinalysis, physical examinations, blood tests and vital signs. | | |
| Statistical Methods: Fisher's test was used due to small sample size (n=62) with an expected number of subjects in each cell of 15 to look for significant difference between the proportions (the number of subjects actually benefited from each treatment). For example, if the proportions are close together the power is small or large if the proportions are far apart. Wilcoxon signed rank test is used for paired groups which are randomly selected from the population. The Mann-Whitney non-parametric test was used to compare two mean scores. A p value of less than 0.05 is considered significant. | | |
| Summary – Conclusions <i>Efficacy Results:</i> Hypertonic solution combined with PicoPrep™ capsules and standard PicoPrep™ are more effective than standard Glycoprep™, and PicoPrep™ capsules alone in cleansing the bowel. Subjects prefer PicoPrep™ capsules alone as a bowel cleansing preparation. <i>Safety Results:</i> There is minimal risk in the use of Hypertonic solution combined with PicoPrep™ capsules as a preparation for colonoscopy when compared to the other preparations. No SAE's were reported. Several AE's were reported, the most common of which were headaches. <i>Conclusions:</i> Hypertonic solution combined with PicoPrep™ capsules is an effective bowel preparation, as rated by doctors and sedationists. The combination is not as well tolerated by subjects as PicoPrep™ capsules alone. Further studies are recommended with larger subject populations. | | |

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1. ABBREVIATIONS AND DEFINITIONS

| | |
|--------|--|
| AE | Adverse Event |
| Ca | calcium |
| CDD | Centre for Digestive Diseases |
| CI | Confidence Interval |
| CRF | Case Report Form |
| CTN | Clinical Trials Notification (Scheme) |
| FBC | Full Blood Count |
| GCP | Good Clinical Practice |
| GI | Gastrointestinal |
| GS | Standard Glycoprep™ sachet |
| HREC | Human Research Ethics Committee |
| HYPC | Hypertonic solution with PicoPrep™ capsules |
| ICH | International Conference on Harmonisation |
| MBA-20 | Full Biochemistry |
| Mg | Magnesium |
| MgO | Magnesium oxide |
| Na | Sodium |
| NaCl | Sodium Chloride |
| NHMRC | National Health and Medical Research Council |
| PCA | PicoPrep™ capsules alone |
| PEG | Polyethylene glycol |
| PS | Standard PicoPrep™ sachets |
| Q1 | First Quarter |
| Q2 | Second Quarter |
| Q3 | Third Quarter |
| Q4 | Fourth Quarter |
| SAE | Serious Adverse Event |
| SIADH | Syndrome of inappropriate secretion of anti-diuretic hormone |
| SSRI | Selective Serotonin Re-uptake Inhibitor |
| SD | Standard Deviation |
| TGA | Therapeutic Goods Administration |

2. ETHICS

2.1 Human Research Ethics Committee (HREC)

Prior to study commencement, the study protocol, patient information and consent document, and any other appropriate documents were submitted to the Centre for Digestive Diseases Human Research Ethics Committee (CDD HREC) Section 12.2.1, with a cover letter listing the documents submitted, their dates of issue, and the site for which approval was sought.

Approval was granted on 22nd March 2004. The CDD HREC was constituted in accordance with the *National Statement on Ethical Conduct in Research Involving Humans* (June 1999) as issued by the National Health and Medical Research Council (NHMRC), in accordance with the NHMRC Act, 1992 (Cth) and ICH Good Clinical Practice (GCP) guidelines (July 2002), at the time of approval.

2.2 Ethical Conduct of the Study

The procedures set out in the study protocol, pertaining to the conduct, evaluation, and documentation of this study, were designed to ensure that the Sponsor and Investigator abide by the principles of the Good Clinical Practice (GCP) guidelines of the ICH and the ethical principles detailed in the current revision of the Declaration of Helsinki (2002). The study was also carried out in keeping with local legal and regulatory requirements.

2.3 Patient Information and Consent

Before being admitted to the clinical study, informed consent was obtained after the nature, scope, and possible consequences of the trial had been explained in a form understandable to the participant.

A Patient Information and Consent document that included study information and participation outline as well as the consent form was prepared. This document complied with all local site and regulatory requirements. The document was written in a language understandable to the subject in layman's terms. The consent form specified who informed the subject. The person who informed the subject and answered queries was either the Investigator or a Research Assistant.

The subject was given the Patient Information and Consent Form, Section 12.2.3 (within appendix of this document), to read. After reviewing the informed consent document and having queries answered, subjects willing to participate were obliged to give consent in writing. The subject's consent was confirmed at this time by the signature of the subject and the person conducting the informed consent discussions. Subjects were consented post pre-screening and before baseline assessments.

3. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Investigators

Dr Thomas Borody (Principal Investigator)*
Dr Antony Wettstein (Co-investigator)~
Dr Sanjay Ramrakha (Co-investigator)#
Dr John Saxon (Co-investigator)^

*~#^ Responsible for final protocol version and determination of assessment criteria. Completion of efficacy assessments.
*~ Informed consent, eligibility, baseline assessments.

Study Manager

Rosa Surace: responsible for overall management of study and monitoring.

Study Co-ordinator

Raquel Llorente: responsible for HREC submission of study documents, preparation of source documents, CRF preparation, IP randomisation and packaging, pre-screening and subject recruitment, consent, subject management, coordination of study visits, subject notes, CRF entry and collation of results.

Please refer to Section 12.2.2 for the curriculum vitae of all study staff.

4. INTRODUCTION

The use of colonoscopic surveillance has increased significantly in recent times as an effective method for detecting colonic polyps and bowel cancer. The effectiveness of this screening relies on an adequately prepared bowel.

Preparation of the bowel has been the most poorly tolerated aspect of colonoscopic procedures. Among the problems encountered are the dietary restrictions of a low residue diet, the period of fasting on the day of the procedure for anaesthetic reasons and, most significantly, the effects of purgative solutions administered on the day prior.

The problems encountered in the bowel preparation phase are due firstly to administration of the preparation itself. Effective bowel preparations as a general rule have poor palatability and frequently result in side effects such as nausea, vomiting, abdominal pain and bloating. Thus palatability and side effects are major factors in the subject's acceptance of the preparation.

Problems in the bowel preparation phase also result from the physiological disturbance of fluid and electrolyte shift, which stem from the purgative effect. Side effects can occur as a result of clinically significant hyponatremia and include confusion, headaches, seizures and comas. Thus physicians are not only concerned with the adequacy of the preparation in cleaning the colon but also with the maintenance of physiological and biochemical parameters.

Effective bowel preparations have yet to achieve acceptance by both parties involved (gastroenterologist and patient).

The initial use of phosphate enemas was associated with significant electrolyte and volume shifts. The introduction of isotonic solutions containing polyethylene glycol (PEG) resulted in safer bowel preparation than phosphate enemas, as these solutions generally result in lower electrolyte shifts. However, isotonic solutions still have significant compliance problems because of poor palatability and the large volume required to achieve adequate bowel preparation.

An alternative to poorly tolerated volumes of solution such as Fleet, PicoPrep™, Picolax and Glycoprep™, has recently been the substitution of encapsulated active ingredients¹. These capsules have been shown to improve palatability².

Another alternative is the use of a hypertonic salt solution, which has been developed to complement the use of existing purgative agents and allows for a reduced volume of the active agent. A reduction in the quantity of any active agent would result in better tolerability and side-effect profile. The addition of the hypertonic salt solution with its dual action can help achieve these objectives without sacrificing quality of the bowel preparation.

The addition of short chain sugar or carbohydrate moieties in the hypertonic salt solution avoids gas formation, bloating and cramps. The various salts as well as the sugar Xylose are used to increase the tonicity of the active solution. The addition of salts also aims to reduce the electrolyte loss during the bowel purgation. However, palatability has been a recurring problem since bowel preparations either taste too salty or are given in too large a volume for easy digestion. This is reduced by using palatable salts such as gluconate, citrate and aspartate, which are known to locally reduce stimulation of salt receptors found on the tongue. Additionally adding flavouring that is complementary to salty dishes may improve palatability.

5. STUDY OBJECTIVES

The aim of this prospective, randomised, single-blinded, comparative study was to assess the efficacy and safety of Hypertonic solution combined with PicoPrep™ capsules (HYPC) as a bowel preparation compared to standard Glycoprep™ (GS), standard PicoPrep™ (PS) and PicoPrep™ capsules alone (PCA). The primary objective was to test the hypothesis that Hypertonic solution combined with PicoPrep™ capsules would be as effective and safe as PicoPrep™ capsules alone, standard PicoPrep™ and standard Glycoprep™ as a bowel preparation. The secondary objective was to assess side effects, patient compliance and tolerance, with the hypothesis that Hypertonic solution combined with PicoPrep™ capsules would be greater tolerated than the other bowel preparations due to lower levels of the active ingredient.

6. INVESTIGATIONAL PLAN

6.1 Overall Study Design and Plan-Description

Design: Randomised, single-blinded, comparative.

Population: The patient population to fully complete the study was to comprise of 60 patients booked to undergo colonoscopic investigation.

Dietary Restriction: All subjects were to refrain from eating solid food on the day prior to colonoscopy and to drink at least one glass of water every hour during and following the bowel preparation, as per standard clinical practice.

Please refer to Section 12.2.3 for study protocol and Section 12.2.4 for sample CRF.

6.2 Discussion of Study Design

No control group was used in this study. This was a comparative study comparing different arms to determine efficacy, safety and tolerance of various bowel preparations. Examinations included urinalysis, blood tests, physical examinations and vital signs as well as Patient, Doctor and Sedationist Evaluation Forms to determine the efficacy, safety and tolerance of the bowel preparations. Throughout the trial, doctors and sedationists were blinded to the preparations study subjects had taken prior to their procedure. It was not possible to blind subject and study co-ordinator from preparations due to the significant differences in dispensation form and instructions for intake.

6.3 Selection of Study Population

6.3.1 Inclusion Criteria

The population base consisted of patients attending the Centre for Digestive Diseases who were scheduled to undergo a colonoscopy. Patients deemed eligible to enter the trial were contacted by telephone up to 14 days before their scheduled procedure and invited to participate. Interested patients were invited to attend the Centre before their scheduled procedure date for study screening purposes. A total of 59 subjects fully completed were to be recruited.

All eligible subjects who were willing to participate in the study were given the opportunity to ask questions, and were thoroughly informed about the study before signing consent.

Subjects who failed to meet the inclusion/exclusion criteria were informed that they were not eligible for the study and would continue under the care of the Investigator as per standard clinical practice. Those who were successfully recruited were given the bowel preparation they were to take once baseline examinations were conducted and eligibility confirmed. All patients who were screened for eligibility were documented regardless of successful recruitment or otherwise.

Patients were required to meet all of the following criteria to be eligible for inclusion in the trial:

1. Males and females aged 18 to 70 years, inclusive.
2. No clinical evidence of any other serious disease (e.g. diabetics) as assessed by the Investigator, which might interfere with the patient's ability to enter the trial.
3. Females must not be pregnant or lactating.
4. Able to communicate well with the Investigators and to comply with the requirements of the entire study. If unable to communicate well with Investigators, translated information sheets / consent forms may be used with a qualified accredited interpreter.
5. Provision of written informed consent to participate.

6.3.2 Exclusion Criteria

Approx. half the exclusion criteria (criteria 1, 3, 7, 8, 11, 13, and 15 to 18) are standard CDD safety exclusion criteria to reduce risks associated with the study and its procedures. Criteria 2, 4 to 6, 12, and 14 were exclusions based on known disorders that may have been exacerbated by the intake of the investigational product. Exclusion criteria 9 and 10 addressed the use of concomitant medications which may have interacted with the investigational product to produce adverse effects.

Patients were excluded for any of the following reasons:

1. Elderly patients with diminished sense of thirst, especially when physical infirmity limits independent access to food and drink.
2. Evidence of pulmonary disease or disorders of the CNS associated with SIADH.
3. Evidence of poor dietary intake / malnutrition as assessed by the investigator.
4. Clinical evidence of hypothyroidism or adrenal insufficiency associated with hypo-osmolar hyponatremia.
5. Known psychiatric patients subject to psychogenic polydipsia.
6. Clinical history of hepatic cirrhosis or congestive heart failure.
7. Clinically relevant abnormalities in physical examination or laboratory screening.
8. Any evidence of significant haematological, hepatic, renal, cardiac, pulmonary, metabolic, neurologic or psychiatric disease.
9. Concurrent medications such as diuretics, indapamide, lithium carbonate, ACE inhibitors, selective serotonin re-uptake inhibitors. Please refer to Section 6.4.4.1 for a complete list of prohibited medications.
10. Concomitant administration of carbamazepine or SSRI both of which can on occasions cause asymptomatic hyponatremia, unless the patient is adequately monitored for these medications.
11. Known acute or chronic renal impairment as assessed by Investigator.
12. Known reaction or sensitivity to monosodium glutamate.
13. Serious adverse reaction or hypersensitivity to any related drug.
14. Asthmatics.
15. Inability to communicate or cooperate effectively with the Investigator or appropriate interpreter.
16. Any contraindication to the colonoscopy procedure.
17. Recent history or current drug or alcohol abuse.
18. Participation in any other clinical trial within the past 30 days.

The exclusion criteria did not greatly inhibit recruitment as the majority of screened patients met the inclusion criteria.

6.3.3 Removal of Subjects from Therapy or Assessment

No subjects were withdrawn due to poor compliance or serious adverse events. One subject was removed from the study and classified as a delayed exclusion upon the return of a positive pregnancy test. Another subject was withdrawn due to anxiety associated with undergoing a colonoscopy. One subject did not complete all study procedures as per protocol due to an adverse event, non-completion of the investigational product and non-assessment by the Doctor and Sedationist. However for the purpose of this study, the subject was included in the Patient

Evaluation and safety analyses. Subjects who were withdrawn were not included in the efficacy assessments.

6.4 Treatments

6.4.1 Treatment Administered

This was a randomised, comparative, single-blinded study. Bowel preparations were administered per arm, with each arm receiving one bowel preparation. The preparations and their doses were as follows:

Tables A: Preparation Administration Schedule

A.1: Arm 1 – Hypertonic Solution with PicoPrep™ capsules

| Time | Hypertonic Solution | PicoPrep™ Capsules | Water |
|------|---|--------------------|---------------|
| 3 pm | 25.015 grams dissolved in 350 ml water | 10 capsules | 6 glasses |
| 6 pm | 0 | 10 capsules | 5 - 6 glasses |

A.2: Arm 2 – PicoPrep™ capsules alone

| Time | PicoPrep™ Capsules | Water |
|------|--------------------|-----------|
| 3 pm | 15 capsules | 6 glasses |
| 9 pm | 15 capsules | 6 glasses |

A.3: Arm 3 – Standard PicoPrep™ sachets

| Time | PicoPrep™ | Water |
|------|-----------|-----------|
| 3 pm | 1 sachet | 6 glasses |
| 9 pm | 1 sachet | 6 glasses |

A.4: Arm 3 – Standard Glycoprep™ sachets

| Time | Glycoprep | Water |
|------|-----------|------------|
| 1pm | 1 sachet | 12 glasses |

Subjects in the standard PicoPrep™ and Glycoprep™ arms followed the standard directions outlined on the packaging for each product.

6.4.2 Identity of Investigational Product

The Hypertonic solution used in this trial contained the following:

Table B.1: Hypertonic Solution Ingredients

| mg/dose | Ingredient |
|-----------|----------------------------------|
| 15.00 | Sodium Picosulphate |
| 10 000.00 | Xylose |
| 5 000.00 | Magnesium Sulphate (epsom salts) |
| 3 000.00 | Sodium Chloride |
| 2 000.00 | Sodium Citrate |
| 2 000.00 | Potassium Gluconate |
| 3 000.00 | Maggi Chicken Flavour |

Table B.2: PicoPrep™ Capsule Ingredients

| g/dose | Ingredient |
|--------|---------------------|
| 10.00 | Sodium Picosulphate |
| 3.50 | Magnesium Oxide |
| 12.00 | Citric Acid |

The PicoPrep™ Capsules were made up from the same powdered ingredients used in Standard PicoPrep™ sachets.

All subjects in Arm 1 received HYPC (this study used batch numbers B0136N, B11181 and C0804). Refer to Section 12.1.7 for a complete breakdown of medication dispensed. No subject received expired bowel preparation at any time during the study.

6.4.3 Selection of Doses in the Efficacy Data

Doses for the bowel preparation were selected and based on standard clinical practice and the optimum minimum dose of active ingredients to successfully empty the bowel without compromising the safety of the subject. Dosages were also based on the dosages available on the market.

6.4.4 Prior and Concomitant Therapy

Additional illnesses present at the time of informed consent was obtained were regarded as concomitant illnesses and were documented on the appropriate pages of the case report form (CRF).

6.4.4.1 Prohibited Medications

The medications prohibited or deemed to interfere with the efficacy of this treatment included diuretics, indapamide, lithium carbonate, carbamazepine, ACE inhibitors and selective serotonin re-uptake inhibitors (SSRIs). Other prohibited medications not classed in the above categories

included amiodarone, chlorpropamine, clofibrate, cyclophosphamide, tolbutamide, thiazides, oxytocin, desmopressin and vincristine.

6.4.4.2 Concomitant Medication

All other concomitant medication for other medical conditions used during the study were recorded in the CRF. This included changes of dose/regimens and/or new treatments. Indication for use was also recorded.

6.4.4.3 Dietary Restrictions

Subjects were asked not to consume any solid food and to drink only clear fluids on the day prior to colonoscopy, as per standard clinical practice. They were required to drink at least one glass of water every hour during and following the bowel preparation.

6.4.5 Treatment Compliance

All bowel preparations were dispensed according to the arm to which each subject was randomised. Bowel preparation was dispensed at Visit 1, and was to be taken prior to colonoscopy, following the instructions given. All bowel preparations were labelled with a batch number and expiry date.

Subjects were instructed to return their bowel preparation packaging at Visit 2 (the day of their colonoscopy). Compliance was assessed by the Patient Evaluation form that each participant was required to complete prior to their procedure and confirmed with the return of empty bowel preparation packaging. Details were recorded in the CRF.

6.5 Efficacy and Safety Variables

6.5.1 Efficacy and Safety Measurements Assessed

Table C: List of Efficacy and Safety Measurements

| EFFICACY | SAFETY |
|-----------------------------|--|
| Doctor Evaluation Form | Physical examination (including vital signs) |
| Sedationist Evaluation Form | Laboratory studies (blood test and urinalysis) |
| Patient Evaluation Form | Adverse events |

The efficacy of the bowel preparations cleansing was measured in all Arms via Doctor and Sedationist Evaluation forms. At each subject's procedure, the Doctor and Sedationist were required to record the overall effectiveness of the bowel preparation used by the subject, on a five-point rating scale ranging from "inadequate" to "excellent". Efficacy of the bowel preparation in cleansing the rectum, terminal ileum, caecum and transverse colon, was also rated by each subject's Doctor and Sedationist, using a rating scale of 1 to 10 (1 = not effective and 10 = highly effective).

Subject compliance and tolerance of the bowel preparation was assessed via subjects' recorded responses on the Patient Evaluation form. The Patient Evaluation form assessed subjects' opinions of the taste of the bowel preparation, ease of completion, ability to complete the preparation, willingness to use the preparation in the future, and perceived efficacy of the preparation.

Safety assessments included physical examinations, laboratory studies (blood tests and urinalysis), vital signs and adverse events. A physical examination was performed and vital

signs assessed for all subjects at Visit 1. At Visit 2, a blood sample and urine sample was collected and vital signs were measured.

Section 9.1 outlines the adverse events recorded over the period of the study. Section 12.1.6 contains a complete list of all adverse events broken down per subject. There were no serious adverse events reported in the duration of the study.

Laboratory results are discussed in Section 9.2, and Section 12.1.8 contains all laboratory results. No deviations from the normal range were deemed clinically significant. One subject was found to be pregnant upon the return of her Visit 1 laboratory results and was excluded from the study.

6.5.2 Appropriateness of Measurements

The Patient Evaluation Form, completed by subjects after taking the bowel preparation and before their colonoscopy, measured the following aspects of the bowel preparations: ease of completion, taste of the preparation, ability to complete the preparation, willingness to use the preparation in the future, and perceived efficacy of the preparation. The evaluation of these aspects of the bowel preparation by subjects is considered a standard efficacy measurement for the evaluation of the tolerability of bowel preparations. Although subject perception of efficacy clearly is of little use, refer to Figure 7, Section 8.4.1.

Both the Doctor Evaluation Form and the Sedation Evaluation Form, completed by doctors and sedationists during colonoscopy to rate the adequacy of the bowel cleansing from 'excellent' to 'poor', are considered standard measurements for evaluating the efficacy of the bowel preparation taken by subjects. However, the 10 point scale of measure introduced too many variables to be of significant statistical value. In addition, Sedationists were included in the efficacy assessments as a means of verifying the Doctor Evaluation. However, in the analysis of efficacy this second set of data reduced the statistical power of the analysis due the varied ratings given by each assessor.

Recording adverse events and the measurement of laboratory values (blood tests and urinalyses) at baseline and after the completion of the bowel preparation are measurements that are commonly used to monitor subject safety when evaluating different bowel preparations.

6.5.3 Data Quality Assurance

Data quality assurance methods implemented for this study include:

- 1) Investigator meeting prior to study commencement,
- 2) Data verification through the use of source documentation,
- 3) Use of a single laboratory for all standard laboratory testing, and
- 4) Monitoring of site files by Study Manager.

6.6 Statistical Methods Planned in the Protocol and Determination of Sample Size

6.6.1 Statistical and Analytical Plans

A total of 62 subjects were screened for study eligibility. Of these 62 subjects were found eligible for study participation and were enrolled into the study. Due to a delayed exclusion, and two withdrawals a total of 59 subjects completed the study. The number of subjects was randomly assigned to each Arm was intended to be 15 per group, however the final numbers differed. The data were analysed for significant difference between preparations using various statistical tests shown in Table D.

Table D: List of Statistical Analyses:

| Statistical Test | |
|---|---|
| Doctor Evaluation (overall adequacy of bowel cleansing) | Differences in Doctor evaluations between arms were analysed using Fisher's exact Test. |
| Sedationist Evaluation (overall adequacy of bowel cleansing) | Differences in Sedationist evaluations between arms were analysed using Fisher's exact Test. |
| Adequacy of Cleansing in Rectum | Differences in Doctor and Sedation evaluations of specific bowel areas between arms were analysed using Mann-Whitney test. |
| Adequacy of Cleansing in Transverse Colon | Differences in Doctor and Sedation evaluations of specific bowel areas between arms were analysed using Mann-Whitney tests. |
| Adequacy of Cleansing in Terminal Ileum | Differences in Doctor and Sedation evaluations of specific bowel areas between arms were analysed using Mann-Whitney test. |
| Adequacy of Cleansing in Caecum | Differences in Doctor and Sedation evaluations of specific bowel areas between arms were analysed using Mann-Whitney test. |
| Patient Evaluation | Differences in Patient evaluations between arms were analysed using Fisher's exact Test. |
| Laboratory Values | Differences between Visit 1 and Visit 2 laboratory values (blood tests and urinalysis) were analysed using the Wilcoxon matched pairs signed rank test. |
| Adverse Events | Differences in adverse events type and severity between arms were analysed using Fisher's exact test. |

6.6.2 Determination of Sample Size

This was a comparative study with a small sample size in order to determine the smallest difference that would be clinically (or scientifically) important for future studies using an appropriate sample size.

6.7 Changes in Conduct of the Study or Planned Analyses

An initial sample size of 60 fully completed subjects was expected, with 15 subjects per Arm. However, only 59 subjects completed the study. This was due to two withdrawals, one of which was not replaced. Not all Arms contained 15 subjects: Arm 1 (HYPC) had 15 subjects, Arm 2 (PCA) had 16 subjects, Arm 3 (PS) had 14 subjects and Arm 4 (GS) had 14 subjects. As this was a comparative study, the sample was not intended to be a statistically significant sample size.

Once the study had been completed and the data correlated, basic statistical analyses were performed. Statistical significance was examined in the following data sets:

1. Differences in doctors' ratings of the overall efficacy of the four bowel preparations and differences in efficacy of the four bowel preparations in the rectum, transverse colon, caecum and terminal ileum (Section 8.4.1).
2. Differences in sedationists' ratings of the overall efficacy of the four bowel preparations and differences in efficacy of the four bowel preparations in the rectum, transverse colon, caecum and terminal ileum (Section 8.4.1).
3. Differences in ratings on ease of completion, taste of preparation, ability to complete preparation, willingness to use preparation in the future and perceived efficacy of the preparation, as reported by participants (Section 8.4.1).
4. Differences between bowel preparations in the type and severity of reported adverse events (Section 8.4.1).

7. STUDY SUBJECTS

7.1 Disposition of Subjects

All enrolled subjects are listed in Table E. This table outlines the details of consent, completion status and reasons for this status. For this study, a total of sixty-two subjects were screened. Two subjects chose to withdraw from the study: one due the anxiety associated with colonoscopy, and the other due to an Adverse Event (severe vomiting) resulting in the subject wishing to cease intake. One subject was deemed a delayed exclusion due to a positive pregnancy test during screening.

Table E: Disposition of Subjects

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Final Visit | Arm | Completion Status | Reason |
|----------------|----------|---------------|----------|----------|-------------|--|-------------------|--------|
| 101 | G-R | 09/08/47 | 17/07/03 | Yes | 21/07/03 | PicoPrep™ Capsules | Completed | N/A |
| 102 | R-R | 18/01/52 | 17/07/03 | Yes | 21/07/03 | PicoPrep™ Capsules | Completed | N/A |
| 103 | YSA | 26/07/50 | 17/07/03 | Yes | 21/07/03 | Standard Glycoprep™ | Completed | N/A |
| 104 | T-D | 08/08/46 | 22/07/03 | Yes | 28/07/03 | Standard PicoPrep™ | Completed | N/A |
| 105 | KGF | 26/04/75 | 24/07/03 | Yes | 31/07/03 | Standard PicoPrep™ | Completed | N/A |
| 106 | S-V | 19/03/64 | 06/08/03 | Yes | 11/08/03 | Standard Glycoprep™ | Completed | N/A |
| 107 | T-C | 25/01/44 | 06/08/03 | Yes | 15/08/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 108 | F-L | 23/05/42 | 07/08/03 | Yes | 12/08/03 | Standard Glycoprep™ | Completed | N/A |
| 109 | M-T | 30/04/44 | 07/08/03 | Yes | 12/08/03 | Standard PicoPrep™ | Completed | N/A |
| 110 | R-G | 23/08/53 | 12/08/03 | Yes | 18/08/03 | PicoPrep™ Capsules | Completed | N/A |
| 111 | BRH | 03/09/63 | 14/08/03 | Yes | 21/08/03 | PicoPrep™ Capsules | Completed | N/A |
| 112 | G-C | 02/03/63 | 14/08/03 | Yes | 18/08/03 | Standard PicoPrep™ | Completed | N/A |
| 113 | R-S | 26/09/71 | 14/08/03 | Yes | 18/08/03 | Standard Glycoprep™ | Completed | N/A |
| 114 | KGT | 28/05/76 | 15/08/03 | Yes | 21/08/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 115 | N-L | 22/05/45 | 18/08/03 | Yes | 22/08/03 | Standard Glycoprep™ | Completed | N/A |
| 116 | A-P | 07/07/77 | 18/08/03 | Yes | 22/08/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 117 | B-D | 31/10/56 | 18/08/03 | Yes | 22/08/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Final Visit | Arm | Completion Status | Reason |
|----------------|----------|---------------|----------|----------|-------------|--|-------------------|-------------------------|
| 118 | JEP | 12/02/38 | 11/09/03 | Yes | 18/09/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 119 | R-W | 11/01/61 | 11/09/03 | Yes | 15/09/03 | Standard Glycoprep™ | Completed | N/A |
| 120 | BAW | 31/01/60 | 12/09/03 | Yes | 17/09/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 121 | MAM | 30/04/70 | 12/09/03 | Yes | N/A | Standard Glycoprep™ | Delayed Exclusion | Positive pregnancy test |
| 122 | SGD | 22/01/56 | 17/09/03 | Yes | 22/09/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 123 | DKH | 28/07/76 | 17/09/03 | Yes | 22/09/03 | Standard Glycoprep™ | Completed | N/A |
| 124 | M-A | 05/01/59 | 17/09/03 | Yes | 24/09/03 | PicoPrep™ Capsules | Completed | N/A |
| 125 | G-W | 04/10/45 | 17/09/03 | Yes | 24/09/03 | PicoPrep™ Capsules | Completed | N/A |
| 126 | AMM | 19/12/62 | 17/09/03 | Yes | 25/09/03 | PicoPrep™ Capsules | Completed | N/A |
| 127 | SJE | 27/04/54 | 19/09/03 | Yes | 26/09/03 | Standard Glycoprep™ | Completed | N/A |
| 128 | ADW | 03/10/56 | 13/10/03 | Yes | 16/10/03 | PicoPrep™ Capsules | Completed | N/A |
| 129 | P-H | 10/06/58 | 16/10/03 | Yes | 20/10/03 | PicoPrep™ Capsules | Completed | N/A |
| 130 | J-S | 31/07/81 | 31/10/03 | Yes | 05/11/03 | Standard PicoPrep™ | Completed | N/A |
| 131 | F-T | 01/01/63 | 06/11/03 | Yes | 10/11/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 132 | KHL | 24/12/44 | 07/11/03 | Yes | 13/11/03 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 133 | JCE | 28/03/57 | 19/01/04 | Yes | 23/01/04 | Standard PicoPrep™ | Completed | N/A |
| 134 | M-M | 20/09/38 | 19/01/04 | Yes | 23/01/04 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 135 | PEB | 30/04/56 | 20/01/04 | Yes | 23/01/04 | PicoPrep™ Capsules | Completed | N/A |
| 136 | FAW | 25/07/54 | 06/02/04 | Yes | 09/02/04 | Standard Glycoprep™ | Completed | N/A |
| 137 | RSM | 29/01/72 | 06/02/04 | Yes | 09/02/04 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 138 | GMC | 25/07/44 | 06/02/04 | Yes | 11/02/04 | PicoPrep™ Capsules | Withdrawn | Subject Request |
| 139 | AEN | 22/04/42 | 09/02/04 | Yes | 11/02/04 | PicoPrep™ Capsules | Completed | N/A |
| 140 | RCW | 02/01/52 | 12/02/04 | Yes | 16/02/04 | Standard PicoPrep™ | Completed | N/A |

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Final Visit | Arm | Completion Status | Reason |
|----------------|----------|---------------|----------|----------|-------------|--|-------------------|-----------------|
| 141 | C-W | 14/04/60 | 12/02/04 | Yes | 19/02/04 | Standard PicoPrep™ | Completed | N/A |
| 142 | G-F | 30/03/43 | 12/02/04 | Yes | 16/02/04 | Standard PicoPrep™ | Completed | N/A |
| 143 | MFB | 14/09/70 | 19/02/04 | Yes | 26/02/04 | Standard PicoPrep™ | Completed | N/A |
| 144 | M-V | 21/08/67 | 19/02/04 | Yes | 24/02/04 | PicoPrep™ Capsules | Completed | N/A |
| 145 | B-W | 06/03/52 | 19/02/04 | Yes | 24/02/04 | Standard PicoPrep™ | Completed | N/A |
| 146 | JAK | 28/03/84 | 20/02/04 | Yes | 26/02/04 | Standard Glycoprep™ | Completed | N/A |
| 147 | P-F | 02/04/67 | 20/02/04 | Yes | 25/02/04 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 148 | SJW | 23/04/71 | 05/03/04 | Yes | 08/03/04 | Standard Glycoprep™ | Completed | N/A |
| 149 | D-C | 26/05/67 | 11/03/04 | Yes | 16/03/04 | Standard PicoPrep™ | Completed | N/A |
| 150 | G-C | 05/11/47 | 11/03/04 | Yes | 15/03/04 | PicoPrep™ Capsules | Completed | N/A |
| 151 | S-A | 06/12/72 | 12/03/04 | Yes | 18/03/04 | Standard Glycoprep™ | Completed | N/A |
| 152 | PGB | 10/03/52 | 15/03/04 | Yes | 17/03/04 | Standard PicoPrep™ | Completed | N/A |
| 153 | AMG | 05/11/35 | 19/03/04 | Yes | 24/04/04 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 154 | P-Q | 13/06/49 | 19/03/04 | Yes | 23/04/04 | Standard PicoPrep™ | Completed | N/A |
| 155 | M-R | 04/12/62 | 26/03/04 | Yes | 31/03/04 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 156 | RST | 14/03/50 | 29/03/04 | Yes | 01/04/04 | PicoPrep™ Capsules | Completed | N/A |
| 157 | C-A | 16/12/74 | 31/03/04 | Yes | 05/04/04 | Standard Glycoprep™ | Completed | N/A |
| 158 | EW P | 08/10/52 | 07/04/04 | Yes | 13/04/04 | PicoPrep™ Capsules | Completed | N/A |
| 159 | D-B | 10/04/46 | 08/04/04 | Yes | 15/04/04 | Hypertonic Solution and PicoPrep™ Capsules | Completed | N/A |
| 160 | A-G | 01/02/61 | 14/04/04 | Yes | N/A | Standard Glycoprep™ | Withdrawn | Subject Request |
| 161 | GRN | 21/08/49 | 19/04/04 | Yes | 23/04/04 | Standard Glycoprep™ | Completed | N/A |
| 162 | M-A | 11/05/59 | 30/04/04 | Yes | 05/05/04 | PicoPrep™ Capsules | Completed | N/A |

7.2 Protocol/Study Procedure Deviations

This study was conducted in compliance with the protocol agreed to by the Sponsor and the Investigator.

Two protocol deviations to the visit schedule occurred. As per visit schedule, Visit 1 procedures must occur 3 days before Visit 2. Both subject 139 (AEN) and subject 152 (PGB) underwent Visit 1 procedures 2 days prior to Visit 2. The protocol waivers were approved by the Sponsor and signed by the Investigator. These deviations were noted in the subject notes and a file note was filed in the subject study file.

The number of completed subjects at the close of the study was 59, instead of 60. It has been determined that this was a result of poor documentation and tracking of subjects, resulting in only one of the two withdrawals being replaced as per the protocol.

Two subjects did not receive the correct IP as per the Randomisation Preparation List. It has been determined that this was due to an error in the preparation of the printed packaging contents. Packaging followed the listed contents as printed on the pack, as such subject 137 received HYPC instead of PS, and subject 139 received PCA instead of HYPC. As a result, an additional subject received PCA instead of PS.

8. EFFICACY EVALUATION

8.1 Data Sets Analysed

The 59 subjects that completed the study were included in the efficacy analyses. Subjects withdrawn from the study were not included in the efficacy analyses, with the exception of the Patient Evaluation data of subject 138, who whilst not completing the study, did in fact take the IP. The data sets analysed for the Patient Evaluation included: taste of preparation, ease of completion, ability to complete preparation, willingness to use preparation in the future and perceived efficacy of the preparation. These evaluations were completed by subjects after taking the preparation and were returned at Visit 2 (Day 3 + 7).

The data sets analysed for the Doctor Evaluation and Sedationist Evaluation included: overall adequacy of bowel preparation, adequacy of preparation in rectum, adequacy of bowel preparation in transverse colon, adequacy of bowel preparation in caecum and adequacy of bowel preparation in terminal ileum. These evaluations were completed by doctors and sedationists during the colonoscopy performed at Visit 2 (Day 3 + 7).

Subjects' previous medical history including any previous colonoscopic procedures was noted as well as the baseline symptoms. These were not analysed for their significance but was noted down for future analyses.

8.2 Demographic and Other Baseline Characteristics

Subjects were from a variety of ethnic backgrounds and countries of birth. The age range of eligible subjects was from 19 (pt # 146) to 68 (pt #153), with the mean age being 45.65 years. The eligible population contained 32 females and 30 males. The average weight at baseline of the male population was 84.22kg, with an average height of 176.42cm. The mean female weight was 65.35kg and height was 162.60cm. The majority (77.42%) of the study population were non-smokers, with 12/62 (19.35%) subjects who smoked daily. Nineteen subjects (30.64%) consumed alcohol on a daily basis, whilst the majority of subjects (32/62, 51.61%) were occasional alcohol drinkers (Section 12.1.10).

All subject medical and demographic history was recorded at baseline (see Section 12.1.3 for PP subjects). Of the 59 subjects who completed the study (PP), it was found that 30/59 subjects had not undergone a colonoscopy at this site before. 5/59 (8.47%) did not have any prior relevant medical history at the time of colonoscopy investigation, 17/59 (28.81%) subjects presented with peri-rectal bleeding. Of the 59 subjects, 10/59 (16.95%) subjects had a history of haemorrhoids. 5/59 (8.47%) subjects had a history of inflammatory bowel disease, and 5/59 (8.47%) had IBS symptoms. 12/59 (20.33%) subjects had previous polypectomies or were found to have pseudo-polyps in the past.

8.3 Measurements of Treatment Compliance

Average compliance for HYPC was 100.0%, PCA was 91.6%, PS was 100.0%, GS was 100.0%, and overall compliance was measured at 97.9% (See Section 12.1.4). Compliance was determined by a study drug count at Visit 2 using the following formulas:

Hypertonic and PicoPrep™ Capsules Compliance (%)

| | | |
|--------|---|----------------------------------|
| Step 1 | $= \frac{(10 - \text{HY weight returned})}{10} \times 10$ | = HY Compliance |
| Step 2 | $= \frac{(30 - \text{no. PC returned})}{20}$ | = PC compliance |
| Step 3 | $= \frac{\text{HY Compliance} + \text{PC compliance}}{2}$ | = Overall per subject compliance |
| Step 4 | $= \frac{\text{Sum of overall per subject compliance}}{14}$ | = Arm 1 Compliance |

| | | |
|--------------------------------|---|--------------------------|
| PicoPrep™ Capsules (%) | | |
| Step 1 | $= \frac{(30 - \text{no. PCA returned})}{30}$ | = Per subject compliance |
| Step 2 | $= \frac{\text{Sum of overall per subject compliance}}{18}$ | = Arm 2 Compliance |
| Standard PicoPrep™ (%) | | |
| Step 1 | $= \frac{(15.546 - \text{PS weight returned})}{15.546}$ | = Per subject compliance |
| Step 2 | $= \frac{\text{Sum of overall per subject compliance}}{14}$ | = Arm 3 Compliance |
| Standard Glycoprep™ (%) | | |
| Step 1 | $= \frac{(200 - \text{GS weight returned})}{200}$ | = Per subject compliance |
| Step 2 | $= \frac{\text{Sum of overall per subject compliance}}{14}$ | = Arm 4 Compliance |
| Overall Compliance (%) | $= \frac{\text{Arm 1} + \text{Arm 2} + \text{Arm 4} + \text{Arm 5}}{4}$ | |

Whilst there was 100% compliance in the PS and GS Arms, subjects commonly complained of poor palatability and difficulty completing. Difficulty in swallowing the large capsules was the claim for poor compliance in the PCA arm. The capsule size was of concern in one subject, who although was able to tolerate the investigational product posed the question of future compliance in other subjects who may have difficulty taking tablets. Difficulty in completing the preparations were directly related to the amount of preparations that needed to be taken, such as the high volume of hypertonic solution and the large amount of PicoPrep™ capsules.

8.4 Efficacy Results

Efficacy data consisted of the following:

1. Doctor Evaluation Form

Doctors assessed the general efficacy of the bowel preparation as well as rating the effectiveness of the bowel preparation in four different areas of the colon (rectum, transverse colon, caecum and terminal ileum).

2. Sedationist Evaluation Form

Sedationists assessed the general efficacy of the bowel preparation as well as rating the effectiveness of the bowel preparation in four different areas of the colon (rectum, transverse colon, caecum and terminal ileum).

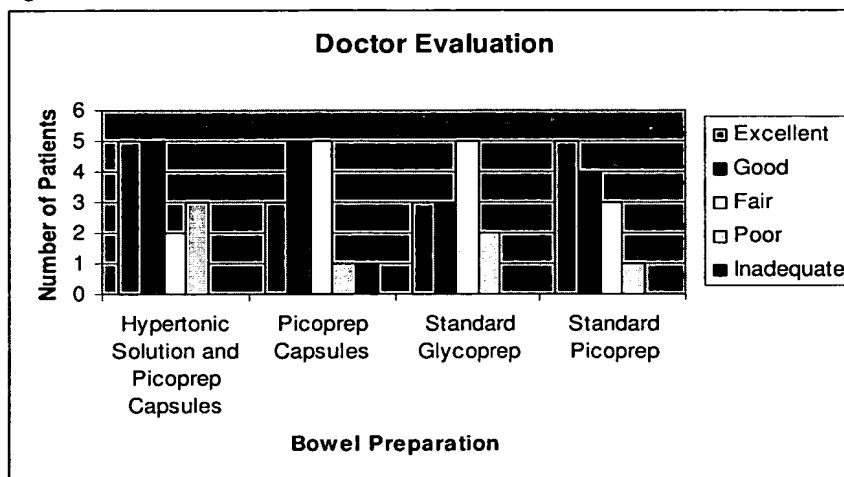
3. Patient Evaluation Form

Subjects evaluated the bowel preparation on five different characteristics: ease of completion, taste of preparation, ability to complete the preparation, willingness to use the preparation in the future and perceived efficacy of the preparation. These formed the basis for assessing subject tolerance of the bowel preparation.

8.4.1 Analysis of Efficacy

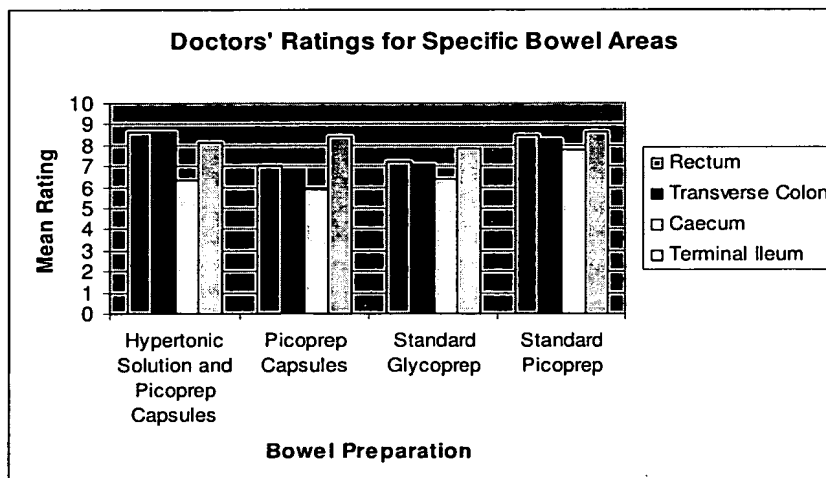
1. Doctor Evaluation

Figure 1



In regards to the general efficacy of each bowel preparation in cleansing the bowel, no significant differences in doctors' ratings of the four bowel preparations were observed. As seen in Figure 1, differences in doctors' ratings of general efficacy of the preparations were minor, with the HYPC (5/15, 33.33%) and the PS Arms (5/14, 35.71%) slightly more often rated as 'excellent' in terms of general efficacy than PCA (3/16, 18.75%) and GS (3/14, 21.42%) arms. See Section 12.1.5.

Figure 2



As seen in Figure 2, doctors' ratings (out of 10) of the adequacy of colonic cleansing for specific bowel areas indicated that HYPC and PS were regarded as more effective in cleansing certain bowel areas than PCA or GS. Significant differences between the arms for the specific bowel areas are outlined below.

1.1 Rectum – No significant differences were observed in the ratings of the efficacy of the four bowel preparations in cleansing the rectum. However a trend, although not significant, was obtained indicating that PS (mean rating = 8.47/10) were more effective than PCA (mean rating = 7.00/10) in cleansing the rectum ($p < 0.06$).

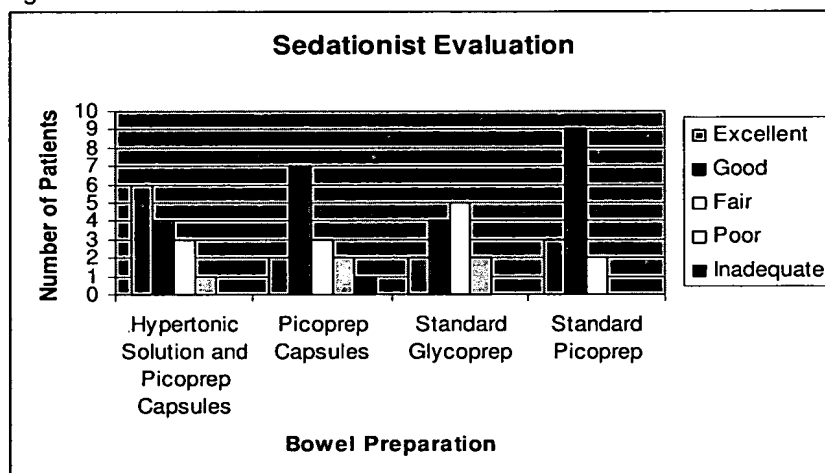
1.2 Transverse Colon – The HYPC bowel preparation (mean rating = 8.60/10) was rated as significantly more effective in cleansing the transverse colon than the PCA bowel preparation (mean rating = 6.68/10, $p < 0.03$). No other significant findings were obtained, however, a trend was observed indicating that PS (mean rating = 8.27/10) was more effective than PCA at cleansing the transverse colon (mean rating = 6.87/10, $p < 0.08$).

1.3 Caecum – Several significant differences were obtained between Arms in terms of adequate cleansing of the caecum. Doctors' ratings indicated that PS (mean rating = 7.80/10) more adequately cleansed the caecum than PCA (mean rating = 5.93/10, $p < 0.03$). Additionally, the HYPC bowel preparation (mean rating = 6.33/10) was found by doctors to be significantly more effective at cleansing the caecum than the PCA bowel preparation (mean rating = 5.93/10, $p < 0.03$).

1.4 Terminal Ileum – No significant differences or trends were observed between the arms in the cleansing the terminal ileum.

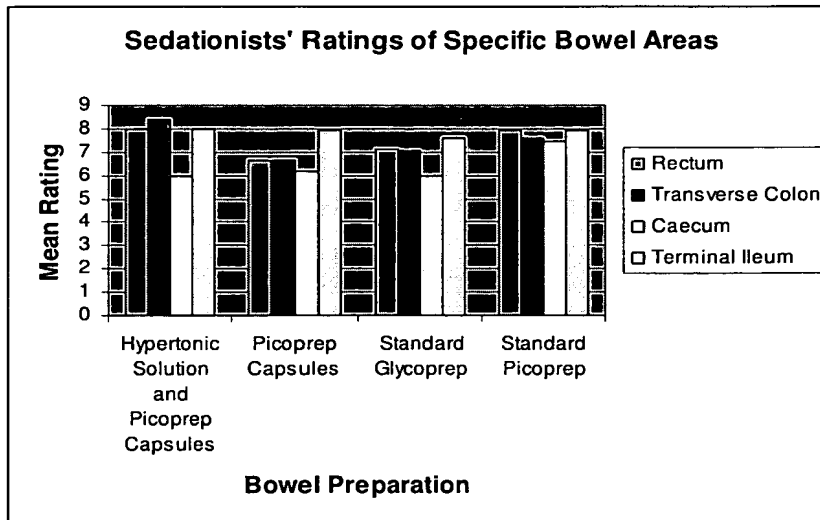
2. Sedationist Evaluation

Figure 3



In regards to the general efficacy of each bowel preparation in cleansing the bowel, no significant differences in sedationists' ratings of the four bowel preparations were observed. As seen in Figure 3, differences in sedationists' ratings of general efficacy of the preparations were minor, with the HYPC arm (6/15, 40.00%) more often rated as 'excellent' in terms of general efficacy than PCA (2/15, 13.33%), GS (2/14, 14.29%) or PS (2/15, 13.33%). See Section 12.1.5.

Figure 4



As seen in Figure 4, sedationists' ratings (out of 10) of the adequacy of colonic cleansing for specific bowel areas indicated that HYPC and PS were regarded as more effective in cleansing certain bowel areas than PCA or GS. Significant differences between the arms for the specific bowel areas are outlined below.

2.1 Rectum – No significant differences were observed regarding the efficacy of the various bowel preparations in cleansing the rectum. However a trend was observed, although not significant, indicating that sedationists viewed PS (mean rating = 7.93/10) as more effective than PCA (mean rating = 6.67/10) in cleansing the rectum ($p < 0.058$).

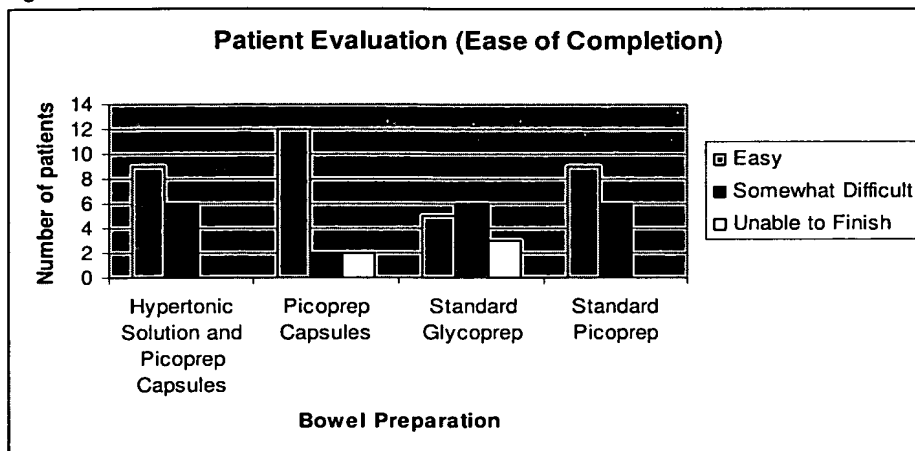
2.2 Transverse Colon – Sedationists rated HYPC (mean rating = 8.40/10) as significantly more effective in cleansing the transverse colon than PCA (mean rating = 6.67/10, $p < 0.03$). Additionally, sedationists ratings indicated that HYPC (mean rating = 8.40/10) was by sedationists as significantly more effective in cleansing the transverse colon than Standard GS (mean rating = 7.07/10, $p < 0.03$).

2.3 Caecum – No significant differences or trends were observed between the arms in the cleansing of the caecum.

2.4 Terminal Ileum – No significant differences or trends were observed between the arms in the cleansing of the terminal ileum.

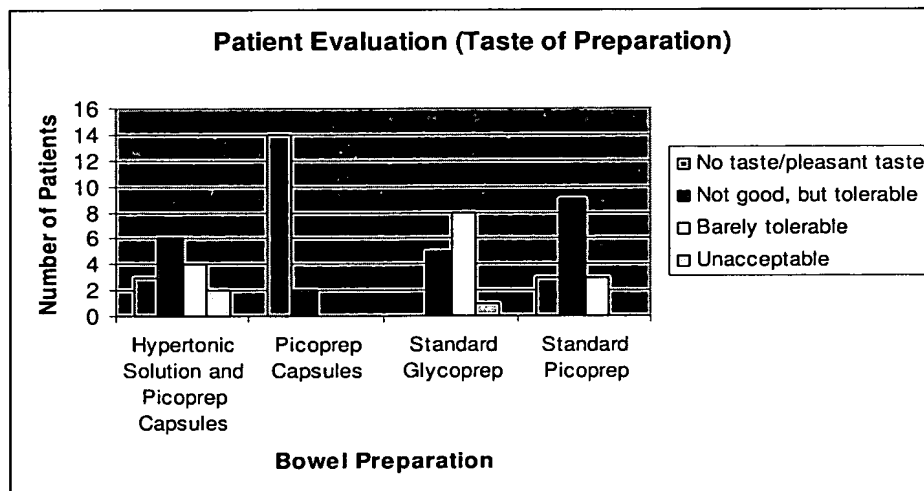
3. Patient Evaluation

Figure 5



As seen in Figure I.5, when compared to the other arms, more subjects in the PicoPrep™ Capsule arm (12/17, 70.58%) rated this bowel preparation as easy to complete. This was significantly different from the Glycoprep™ arm, in which only 5/14 subjects (35.71%), rated the preparation as easy to complete ($p < 0.03$). No other significant differences or trends were observed for the ease of completion between the four bowel preparations. See Section 12.1.5.

Figure 6

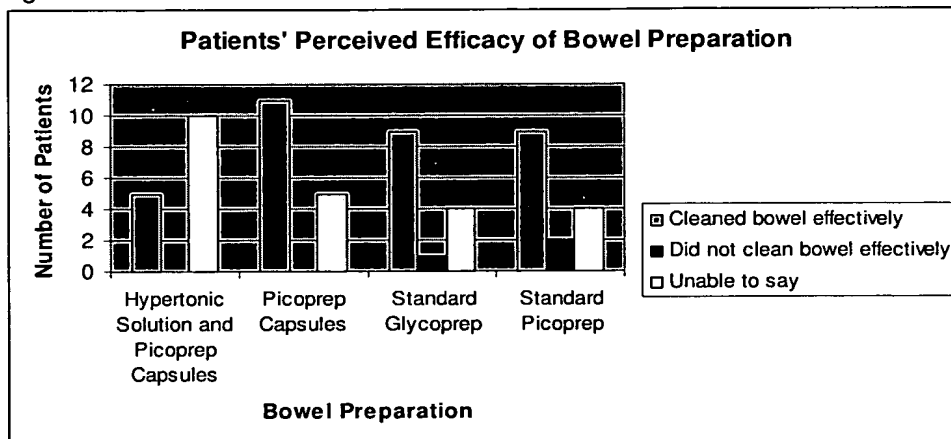


A number of significant findings were obtained regarding subjects' ratings of the taste of the four bowel preparations. Figure 6 demonstrates that the majority of subjects in the PCA arm (14/17, 82.35%) rated the preparation as having a pleasant or nil taste. This was significantly different from the GS preparation in which no subjects rated the taste as pleasant ($p < 0.0001$), the HYPC arm, in which 3/15 subjects (20.00%) rated this preparation as having a pleasant or nil taste ($p < 0.0002$), and the PS arm, in which 3/14 subjects (21.43%) rated this preparation as having a pleasant or nil taste.

Additionally, significantly more subjects in the GS arm (8/14, 57.14%) rated their preparation as barely tolerable compared to subjects in the PCA arm (0/17, $p < 0.0008$), and significantly more

subjects in the PS arm (9/14, 64.29%) rated their preparation as not good but tolerable, compared to those in the PCA arm (2/17, 11.76%, $p < 0.021$). No other significant findings or trends were observed for subjects' ratings of the taste of the bowel preparations.

Figure 7



While no significant findings were obtained for subject's ratings of perceived efficacy of the bowel preparations, several trends were observed. As demonstrated in Figure 7, more subjects in the HYPC arm (10/15, 66.67%) were unable to state how effective they found the bowel preparation compared to subjects in the PS (4/14, 28.57%, $p < 0.07$), GS (4/14, 28.57%, $p < 0.07$) and PCA (5/17, 29.41%, $p < 0.07$) arms. Additionally, more subjects in the PCA arm (11/17, 64.71%) thought that their preparation cleaned their bowel effectively compared to those in the HYPC arm (5/15, 33.33%, $p < 0.07$). This data has no clear correlation with the Doctor and Sedationist Evaluations.

8.4.2 Handling of Drop-outs and Missing Data

The data from the ITT group (screening failures, delayed exclusions and withdrawals) were not collated and analysed within the efficacy data, with the exception of the Patient Evaluation of subject 138.

A single subject was classified as a delayed exclusion. This subject did not receive any bowel preparation and did not undergo a colonoscopy, as the Baseline Visit blood test results revealed subject was pregnant. Subject returned all study medication and the unused Patient Evaluation Form upon receiving the news. As such, the subject was not included in any efficacy and safety analyses.

One withdrawn subject (160) at study Visit 2 due to anxiety associated with concern of undergoing a colonoscopic evaluation. Subject had undergone all screening procedures, but did not take any bowel preparation. As such, the subject was not included in any efficacy and safety analyses.

Missing data points in the laboratory studies resulted in the subjects' removal from that data set (i.e. specific tests) analysis as only 2 data points are involved.

8.5 Efficacy Conclusions

Doctor Evaluation

In the overall adequacy of colon cleansing, doctors found no difference between the preparations used. However, when looking at specific areas of the colon, several differences arose between the four bowel preparations. Doctors rated both PS and HYPC as being more

effective in cleansing the caecum than PCA. Additionally, doctors rated HYPC as more effective than PCA when cleansing the transverse colon.

The two trends that were observed demonstrated that doctors rated PS as more effective than PCA when cleansing the rectum and the transverse colon. While these findings only approached significance, a larger sample size may result in significant findings.

Sedationist Evaluation

In the overall adequacy of cleansing, sedationists found no difference between the bowel preparations used. However, when looking at specific areas of the colon, several differences arose between the four preparations. Sedationists rated the HYPC as more effective in cleansing the transverse colon than the GS preparation. The HYPC preparation was also rated by sedationists as more effective in cleansing the transverse colon than PCA.

In addition to these findings, two trends were observed, illustrating that sedationists rated PS as more effective in cleansing the rectum and caecum than PCA. These trends did not reach significance, but with a larger sample size these differences may become significant.

The differences noted between the Doctor and Sedation Evaluations may result from a number of factors, such as: Sedationists need to tend to the subject during the procedure, thus drawing their attention from the viewing screen, or Sedationists not trained like a gastroenterologist to identify where in the colon the colonoscope currently resides, thus misinterpreting the assessments points.

Patient Evaluation

The PCA bowel cleansing preparation was the preparation that was best tolerated by subjects prior to colonoscopy. Subjects reported that they found this preparation easier to complete than GS and it was also found that subjects preferred the taste of PCA to the taste of GS, PS, and the HYPC preparation. Additionally, more subjects in the GS arm rated the taste of the preparation as only barely tolerable compared to PCA and more subjects in the PS arm rated this preparation as not good, but tolerable compared to subjects in the PCA arm. Subjects' reports of greater tolerability of the PCA bowel preparation may be due to the texture and taste of the other preparations.

Non-significant trends indicated that subjects viewed PCA as more effective at cleansing the bowel than HYPC. In addition, more subjects in the HYPC arm were unsure of the efficacy of their preparation compared to those taking PCA, PS or GS. While these differences in perceptions of efficacy of the various bowel treatments only approached significance, they may reflect trends that could become significant with a larger sample size. The uncertainty that subjects had concerning the efficacy of the HYPC preparation may be an indication of subjects' reactions to a new bowel preparation that is not yet available on the market, compared to GS or PS which are both readily available and widely known.

Conclusion

These findings indicate that overall, PCA were most favoured as a bowel preparation by subjects. However, doctors and sedationists generally rated the efficacy of Hypertonic Solution and PicoPrep™ Capsules, and PS as more effective than the other preparations in cleansing the bowel.

9. SAFETY EVALUATION

9.1 Adverse Events

9.1.1 Summary of Adverse Events

A total of 30 subjects reported adverse events over the duration of their participation in the study. Several subjects reported experiencing more than one adverse event over the course of the study, resulting in a total of 44 adverse events being reported by 30 subjects. Of the adverse events reported, 47.7% (21/44) were headaches and 18.1% (8/44) of the adverse events reported were gastrointestinal (e.g. vomiting, nausea or bloating). The majority of these AE's (25/44, 56.8%) were assessed as "probably related" to the bowel preparation taken, and a further 25.0% (11/44) of the adverse events reported were assessed as "possibly related" to the bowel preparation.

As part of the safety analyses, the number, type and severity of adverse events were separated according to the bowel preparation taken by the subject and compared with the other bowel preparations. Several significant differences between the bowel preparations in terms of the number, type and severity of adverse events reported was observed. Refer to Section 12.1.6 for tabulated data. Of particular note HYPC resulted in no nausea, vomiting, bloating, and faint/light headedness in any subject. In addition, the PCA and PS arms had a similar adverse event profile in the moderate/severe AE's, a marked difference in the number of headaches experienced in the mild AE's. 4/14 (28.57%) PS subjects experienced mild headaches, whereas only 1/16 (6.25%) of PCA subjects did ($p=0.17$).

9.1.1.1 PicoPrep™ Capsules vs. Standard Glycoprep™

There were no significant difference between PCA and GS in the number and type of moderate and severe adverse events that were reported by subjects. However, a statistically significant difference was observed between the two groups in regards to the number of mild adverse events that subjects experienced, with subjects in the GS group (6/14, 42.86%) reporting a significantly higher number of mild adverse events than in the PCA group (1/16, 6.25%) ($p < 0.031$). No significant differences were observed between the two bowel preparation groups in terms of the type of mild adverse events that subjects reported. A non-significant trend was observed in the event of mild headache there were 4/14 (28.57%) GS subjects versus 1/16 (6.25%) ($p=0.33$) PCA subjects experiencing this event.

The most common adverse events experienced overall by subjects using GS were headaches (5/14, 36%) and vomiting (2/14, 14.29%). The most common adverse events experienced by subjects using PCA were headaches (3/16, 18.75%) and vomiting (2/16, 12.50%).

9.1.1.2 PicoPrep™ Capsules vs. Standard PicoPrep™

There were no significant differences between the PCA preparation and the PS preparation in the number of moderate and severe adverse events that subjects reported. However, a significant difference was observed between the two groups in the number of mild adverse events that subjects experienced, with subjects in the PS arm (6/14, 42.86%) reporting a significantly higher number of mild adverse events than subjects in the PCA arm (1/16, 6.25%) ($p < 0.037$). No statistically significant difference was observed between the two preparation groups in the type of adverse events that subjects experienced. A non-significant trend observed in the event of mild headache there was 4/14 (28.57%) PS versus 1/16 (6.25%) ($p=0.17$) PCA subjects experiencing this event. The reason for this difference is unclear, given that the components of the two products are identical, it is only the delivery method which differs. Reasons for this difference may be a result of subjects taking PCA may be more likely to drink more water with the capsules than those who are taking PS and already having to consume 2L of a thick fluid before additional water intake.

The most common adverse events overall experienced by subjects using PCA were headaches (3/16, 18.75%) and vomiting (2/16, 12.50%). The most common adverse events overall experienced by subjects using PS were headaches (5/14, 35.71%) and faint / light headedness (2/14, 14.28%).

9.1.1.3 PicoPrep™ sachets vs. Hypertonic Solution and PicoPrep™ Capsules

There were no significant differences between the PS preparation and the HYPC preparation in the number and type of moderate and severe adverse events. Similarly, there were no significant differences between the two groups in the number or type of mild adverse events that subjects experienced. Two non-significant trends were observed; firstly in the event of moderate-severe headache there were 4/15 (26.66%) HYPC versus 1/14 (7.14%) (p=0.32) PS subjects experiencing this event, and secondly in the event of moderate-severe faint / light headedness, there were 2/14 (15.38%) PS versus 0/15 (0.00%) (p=0.48) HYPC.

The most common adverse events reported by subjects using HYPC were headaches (8/15, 53.33%) and faint / light headedness (1/15, 6.66%). The most common adverse events reported by subjects using PS were headaches (5/14, 35.71%) and faint / light headedness (2/14, 14.28%).

9.1.1.4 PicoPrep™ capsules vs. Hypertonic Solution and PicoPrep™ Capsules

There were no significant differences between the PCA preparation and the HYPC preparation in the number and type of moderate and severe adverse events. A non-significant trend observed in the event of moderate-severe headache, with 4/15 (26.66%) HYPC versus 2/16 (12.50%) (p=0.39) PCA subjects experiencing this event.

Similarly, there were no significant differences between the two groups in the number and type of mild adverse events that subjects experienced. However a non-significant trend was observed regarding the number of mild adverse events that subjects experienced. Subjects taking the HYPC (5/15, 33.33%) reported more mild adverse events than those using the PCA (1/16, 6.25%) (p < 0.083). Another non-significant trend regarding the type of adverse events that subjects experienced was observed, indicating that subjects in the HYPC arm (8/15, 53.33%) reported experiencing more headaches than subjects in the PCA arm (3/16, 18.75%) (p < 0.066).

The most common adverse events reported by subjects using HYPC were headaches (8/15, 53.33%) and faint / light headedness (1/15, 6.66%). The most common adverse events experienced by subjects using PCA were headaches (3/16, 18.75%) and vomiting (2/16, 12.5%).

9.1.1.5 Glycoprep™ sachets vs. Hypertonic solution combined with PicoPrep™ capsules

There were no significant differences between the GS preparation and the HYPC preparation in the number of moderate and severe adverse events that subjects reported. However a non-significant trend showed that more subjects reported moderate-severe headaches in the HYPC arm (4/15, 26.66%) than in the GS arm (1/14, 7.14%) (p=0.17).

Similarly, there were no significant differences between the two groups in the number of mild adverse events that subjects experienced. However, a significant difference was observed between the two groups in the type of adverse events that subjects experienced, with subjects using GS (2/14, 14.28%) reporting a higher number of gastroenterological adverse events (e.g. vomiting and nausea) than those taking HYPC (0/15, 0.00%) (p < 0.0001). The most common adverse events reported by subjects using HYPC were headaches (8/15, 53.33%) and faint / light headedness (1/15, 6.66%). The most common adverse events experienced by subjects using GS were headaches (5/14, 35.71%) and vomiting (2/14, 14.29%).

9.2 Clinical Laboratory Evaluation

There were no significant findings in the haematological laboratory results for the GS and PS arms. The PCA and HYPC arms saw statistical significance when leucocyte values were compared from Visit 1 and Visit 2 (PCA p=0.035, HYPC p=0.002). However these were determined to be of no clinical significance as a number of underlying concomitant conditions existed in the Study subjects. The PCA arm also yielded statistically significant values when platelet counts obtained at Visit 1 and Visit 2 were compared, however these were also

considered to be of no clinical significance. There were no significant changes noted in the serum electrolyte levels, in particular serum sodium, nor in serum osmolality.

Urinalysis demonstrated a number of significant changes. Urine electrolyte changes varied in each arm. Sodium levels in each arm did not demonstrate a statistically significant change, and any changes seen (HYPC Visit 1 92.73 ± 36.76 and Visit 2 68.93 ± 45.08 ; GS Visit 1 109.13 ± 54.67 and Visit 2 126.46 ± 62.11) were within normal range. As the levels of urine sodium were less than 200mmol/L this suggests that in these euvolaemic patients with intact renal function, changes were due to gastrointestinal loss.

PCA arm demonstrated statistically and clinically significant decrease in urine potassium levels between Visit 1 (mean \pm standard deviation) (86.81 ± 51.61) and Visit 2 (42.13 ± 38.32) $p=0.016$, however still within normal range (25-75mmol/L). The urine chloride levels also demonstrated a statistically and clinically significant decrease from Visit 1 (138.93 ± 59.45) to Visit 2 (78.91 ± 46.05) $p=0.014$, normal range being 122-135mmol/L. The mean chloride level reduced from the normal range to a level significantly below the acceptable normal range.

The HYPC arm demonstrated statistically and clinically significant decreases in urine potassium Visit 1 (69.13 ± 29.93) to Visit 2 (42.40 ± 27.42) $p=0.013$, normal range being 25-75mmol/L. Urine chloride levels also demonstrated a statistically and clinically significant decrease from Visit 1 (122.73 ± 46.97) to Visit 2 (73.14 ± 40.97) $p=0.032$, normal range being 122-135mmol/L. The mean urine chloride level reduced from slightly below normal range to a level significantly below the acceptable normal range. This suggests chloride retention and therefore reduced urine chloride loss.

The PS arm demonstrated a statistically significant decrease in urine potassium levels from Visit 1 (76.00 ± 52.97) and Visit 2 (27.71 ± 25.81) $p=0.017$, normal range being 25-75mmol/L. Prior to intake of preparation urine excretion of potassium, while within the normal range, had variation across the range and above. However there was a significant decrease in excreted urine potassium following ingestions of preparation. It can be deduced that potassium is selectively reabsorbed in normally functioning kidneys, in an attempt to maintain serum potassium concentration. No significant change was seen in serum potassium.

The GS arm demonstrated a statistically significant change in chloride levels from Visit 1 (122.13 ± 60.14) and Visit 2 (75.73 ± 35.36) $p=0.064$, normal range being 122-135mmol/L. The mean chloride level reduced from the low end of normal range to a level significantly below the acceptable normal range.

Osmolarity measures the kidneys ability to concentrate/dilute urine in fluctuating conditions. Changes in Specific Gravity indicate a change in the concentration of urine. The subjects taking PCA demonstrated statistically significant decreases in both. Changes in osmolality from Visit 1 (736.06 ± 220.22) to Visit 2 (539.13 ± 198.99) $p=0.011$, with normal range being 100-800mmol/Kg. The specific gravity decreased from Visit 1 (1.019 ± 0.006) to Visit 2 (1.015 ± 0.005) $p=0.017$, with normal range being 1.005-1.030. The subjects taking HYPC demonstrated statistically significant changes in both osmolality and specific gravity. Changes in osmolality from Visit 1 (655.00 ± 227.88) to Visit 2 (442.73 ± 229.11) $p=0.013$, with normal range being 100-800mmol/Kg. The specific gravity from Visit 1 (1.018 ± 0.006) to Visit 2 (1.013 ± 0.007) $p=0.091$, with normal range being 1.005-1.030.

These changes were statistically and clinically significant. This indicates that the kidneys ability to alter the concentration in various conditions is not impaired. The less osmolar, and therefore less concentrated urine, were noted with associated decreases in urine chloride concentration in the above groups.

Subjects taking PS and GS showed no statistically or clinically significant changes in osmolality or specific gravity. Indicating that neither of these preparations effect these measures.

Differences in urine osmolality and urine potassium and chloride levels in the HYPC arm was less than the PCA arm, although the PCA arm had higher than usual baseline values. Whereas

PS and GS, showed little change with the exception of a negative change in one of the electrolytes.

9.3 Vital Signs, Physical Findings, and other Observations related to Safety

Physical examinations were only performed at Visit 1(PP). Of the physical examinations performed, 1/59 had faecal loading of the right colon at baseline, 1/59 reported abdominal tenderness at baseline. However these two conditions did not affect subjects' participation in the study. 5/59 subjects reported other conditions not clinically significant to the study (basal cell carcinoma, acne rosacea, shoulder rash, multiple solar keratosis cell carcinoma). Vital signs remained within normal ranges for Visit 1 and 2, and there were no major weight deviations in any arm between Visit 1 and 2.

9.4 Safety Conclusions

No adverse event was classed as serious or deemed definitely related to the investigational product. Overall, more subjects reported adverse events on GS (57.14%), than PCA (50.00%), HYPC (46.66%) and PS (41.17%). However, the adverse events in the PC arm were generally milder than any of the other arms.

Haematological results showed no significant trends or dramatic changes within parameters. Urine osmolarity decrease was reflected by a decrease in urine excreted potassium and chloride concentrations in the HYPC and PCA arms. There was less of a decrease in the HYPC arm, perhaps a reflection of the hypertonic solutions influence. It is of note that there were a greater number of headaches reported in these two groups.

PCA and PS had the same composition but delivered differently, however the results of the safety assessments differ. This may be a result of relative water intoxication. While the GS arm demonstrates the inert nature of PEG products.

10. DISCUSSION AND OVERALL CONCLUSIONS

Hypothesis

In evaluating the efficacy and safety of HYPC compared with PCA, GS, and PS as a bowel preparation, the hypotheses that HYPC would be better tolerated by subjects, would have a better side effect profile and would be as effective in cleansing the bowel as the other bowel preparations were tested.

Efficacy

The efficacy data demonstrates that while doctors and sedationists did not significantly differentiate between the different bowel preparations in the overall adequacy of bowel cleansing, when rating the cleanliness of the bowel according to specific bowel areas (i.e. rectum, transverse colon, caecum and terminal ileum), both agreed that HYPC was more effective in cleansing the transverse colon than the other bowel preparations. Doctors rated this preparation as significantly more effective than PCA, and sedationists rated this preparation as more effective than GS and PS in cleansing the transverse colon. Additionally, doctors rated both HYPC and PS and as being more effective in cleansing the caecum than PCA. While the ratings given to the efficacy of different bowel preparations varied slightly between doctors and sedationists, overall, doctors and sedationists agreed on the efficacy of the different preparations in cleansing various areas of the bowel. In general, both doctors and sedationists rated the efficacy of PS and HYPC as superior to PCA and GS. In the instances where doctors found significant differences between the preparations that sedationists did not, or vice versa, both agreed on which were the better preparations with only a few rating points determining significance.

HYPC preparation was equal or superior in efficacy, as assessed by the doctors and sedationists, compared to the other bowel preparations. When rating the preparations for tolerability, subjects reported that the PCA preparation was the most tolerable preparation to take prior to colonoscopy. Subjects appear to have found this preparation easier to complete than the GS preparation, and they stated that they preferred the taste of PCA to the taste of the GS, PS, and the HYPC.

Overall, the most overall efficacious bowel preparation would be HYPC, followed by PS. The most efficacious in subject tolerability is PCA.

Safety

The safety data suggests that while approximately half of the subjects in the HYPC arm experienced side effects that were possibly related to the bowel preparation, these adverse events were mostly mild. However the data suggests that PS results in fewer side effects, but PCA results in milder side effects. No serious adverse events were reported in any of the arms.

HYPC and PCA do not cause any significant clinical changes in laboratory results, except in urine chloride. However these results suggest that GS is the least likely to cause shifts in laboratory values.

Future Studies

While these results suggest that HYPC are highly effective in cleansing of the bowel, future studies should explore methods of reducing the side effect profile of the preparation, particularly reducing the amount of headaches subjects experience when taking the preparation. Additionally, improving the taste of the preparation would also assist in improving compliance and ease of completion as reported by subjects taking the preparation, and should be focused on in future studies.

In addition, to improve data clarity, a statistically significant subject population should be used, and only the Doctor should evaluate the efficacy of the bowel preparation, using a 5 point scale rather than 10.

Conclusions

These findings indicate that overall, PCA were most favoured as a bowel preparation by subjects, and, in general, resulted in a lower number of mild adverse events than the other preparations. However, doctors and sedationists generally rated the efficacy of HYPC, and PS as more effective than the other preparations in cleansing the bowel. Future studies should be considered to increase the population size to statistical significance

11. REFERENCE LIST

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2. Fincher RK, Osgard EM, Jackson JL, Strong JS, Wong RKA. Comparison of bowel preparations for flexible sigmoidoscopy: oral magnesium citrate combined with oral bisacodyl, one hypertonic phosphate enema, or two hypertonic phosphate enemas. *American Journal of Gastroenterology* 1999; 94(8): 2122-7.

12. APPENDICES

12.1 Subject Data Listings

12.1.1 Discontinued Subjects and Protocol Deviations

| Patient No. | Sex | Age | Discontinued or Deviation | Reason for discontinuation or Protocol deviation |
|-------------|--------|-----|---|---|
| 121 | Female | 33 | Discontinued | Delayed Exclusion – positive pregnancy test. |
| 137 | Male | 32 | Deviation from randomisation schedule | Incorrect labelling of randomised packaging |
| 138 | Female | 59 | Discontinued | Withdrawn – Adverse Event |
| 139 | Female | 61 | Deviation from visit schedule and from randomisation schedule | Performed Visit 1 procedures 2 days prior to Visit 2 (must be 3 days), and incorrect labelling of randomised packaging. |
| 152 | Male | 52 | Deviation from visit schedule | Performed Visit 1 procedures 2 days prior to Visit 2 (must be 3 days) |
| 160 | Male | 43 | Discontinued | Withdrawn – did not undergo colonoscopy. |

12.1.2 List of Subjects Excluded from Efficacy Analysis

| Patient No. | Sex | Age | Reason Excluded from Efficacy Data |
|-------------|--------|-----|--|
| 121 | Female | 33 | Delayed Exclusion – positive pregnancy test. |
| 138 | Female | 59 | Withdrawn – AE, unable to complete preparation.* |
| 160 | Male | 43 | Withdrawn – did not undergo colonoscopy. |

* Included in Patient Evaluation only.

12.1.3 Demographic Data

| Patient Number | Initials | Sex | DOB | Age at Consent | Ethnicity | Country of Birth | Smoking Status | Alcohol | Pregnancy | Height (cm) | Weight at Baseline (Kg) |
|----------------|----------|-----|----------|----------------|-----------|------------------|----------------|------------|-----------|-------------|-------------------------|
| 101 | G-R | M | 09/08/47 | 56 | Caucasian | Australia | Non | Daily | N/A | 188.0 | 105 |
| 102 | R-R | M | 18/01/52 | 51 | Asian | Hong Kong | Daily | Daily | N/A | 182.8 | 75.5 |
| 103 | YSA | M | 26/07/50 | 53 | Hispanic | Peru | Non | Occasional | N/A | 153.0 | 51.5 |
| 104 | T-D | F | 08/08/46 | 57 | Caucasian | Australia | Non | Daily | N/A | 180.3 | 102.0 |
| 105 | KCF | M | 26/04/75 | 28 | Caucasian | N/A | Daily | Occasional | Negative | 168.0 | 65.5 |
| 106 | S-V | F | 19/03/64 | 39 | Caucasian | India | Non | Occasional | Negative | 155.0 | 65.1 |
| 107 | T-C | F | 25/01/44 | 59 | Caucasian | Australia | Non | Never | Negative | 170.0 | 65.4 |
| 108 | F-L | M | 23/05/42 | 61 | Caucasian | Australia | Non | Daily | N/A | 171.5 | 73.3 |
| 109 | M-T | F | 30/04/44 | 59 | Caucasian | Australia | Non | Daily | Negative | 180.0 | 58.0 |
| 110 | R-G | M | 23/08/53 | 49 | Caucasian | Australia | Non | Occasional | N/A | 177.0 | 85.5 |
| 111 | BRH | M | 03/09/63 | 39 | Caucasian | Australia | Non | Occasional | N/A | 178.0 | 85.0 |
| 112 | G-C | M | 02/03/63 | 40 | N/A | Australia | Daily | Daily | N/A | 180.0 | 88.5 |
| 113 | R-S | M | 26/09/71 | 31 | Caucasian | Australia | Non | Occasional | N/A | 181.0 | 100.0 |
| 114 | KGT | M | 28/05/76 | 27 | Caucasian | N/A | Non | Occasional | N/A | 178.0 | 85.0 |
| 115 | N-L | M | 22/05/45 | 58 | N/A | Egypt | Non | Occasional | N/A | 185.4 | 93.5 |
| 116 | A-P | F | 07/07/77 | 26 | Caucasian | Australia | Non | Occasional | Negative | 173.0 | 70.0 |
| 117 | B-D | F | 31/10/56 | 46 | Asian | Hong Kong | Non | Never | Negative | 155.0 | 54.0 |
| 118 | JEP | F | 12/02/38 | 65 | Caucasian | Australia | Non | Daily | N/A | 165.0 | 63.6 |
| 119 | R-W | M | 11/01/61 | 42 | Caucasian | Australia | Occasional | Occasional | N/A | 187.0 | 95.5 |
| 120 | BAW | F | 31/01/60 | 43 | Caucasian | Australia | Non | Occasional | Negative | 168.0 | 83.0 |
| 121 | MAM | F | 30/04/70 | 33 | Hispanic | Australia | Daily | Daily | Positive | 162.5 | 74.0 |
| 122 | SGD | M | 22/01/56 | 47 | Caucasian | China | Occasional | Never | N/A | 180.0 | 89.0 |
| 123 | DKH | F | 28/07/76 | 27 | Caucasian | Australia | Daily | Occasional | Negative | 166.0 | 54.5 |

| Patient Number | Initials | Sex | DOB | Age at Consent | Ethnicity | Country of Birth | Smoking Status | Alcohol | Pregnancy | Height (cm) | Weight at Baseline (Kg) |
|----------------|----------|-----|----------|----------------|-----------|------------------|----------------|------------|-----------|-------------|-------------------------|
| 124 | M/A | F | 05/01/59 | 44 | Caucasian | Australia | Non | Occasional | Negative | 155.0 | 60.5 |
| 125 | G-W | M | 04/10/45 | 57 | Caucasian | Australia | Non | Occasional | N/A | 180.0 | 92.5 |
| 126 | AMM | F | 19/12/62 | 40 | Caucasian | Australia | Non | Daily | Negative | 155.0 | 79.0 |
| 127 | SJE | F | 27/04/54 | 49 | Caucasian | Australia | Non | Occasional | Negative | 174.0 | 58.2 |
| 128 | ADW | M | 03/10/56 | 47 | Caucasian | United Kingdom | Non | Daily | N/A | 185.0 | 87.5 |
| 129 | P-H | M | 10/06/58 | 45 | Caucasian | Australia | Non | Daily | N/A | 175.0 | 80.6 |
| 130 | J-S | F | 31/07/81 | 22 | Caucasian | Australia | Daily | Occasional | Negative | 165.0 | 63.2 |
| 131 | F-T | M | 01/01/63 | 40 | Caucasian | Australia | Non | Occasional | N/A | 163.0 | 80.1 |
| 132 | KHL | M | 24/12/44 | 58 | Asian | China | Non | Never | N/A | 170.0 | 74.0 |
| 133 | JCE | F | 28/03/57 | 46 | Caucasian | Australia | Non | Never | Negative | 157.5 | 66.5 |
| 134 | M-M | M | 20/09/38 | 65 | Caucasian | Australia | Non | Daily | N/A | 177.8 | 95.2 |
| 135 | PEB | M | 30/04/56 | 47 | Caucasian | Australia | Non | Occasional | N/A | 178.0 | 78.2 |
| 136 | FAW | F | 25/07/54 | 49 | Caucasian | Australia | Non | Occasional | Negative | 170.0 | 58.5 |
| 137 | RSM | M | 29/01/72 | 32 | Caucasian | Australia | Daily | Daily | N/A | 187.5 | 92.5 |
| 138 | GMC | F | 25/07/44 | 59 | Caucasian | Australia | Non | Never | Negative | 162.5 | 56.8 |
| 139 | AEN | F | 22/04/42 | 61 | Caucasian | Australia | Daily | Daily | Negative | 175.0 | 76.5 |
| 140 | RCW | F | 02/01/52 | 52 | Caucasian | Australia | Non | Occasional | N/A | 160.0 | 68.5 |
| 141 | C-W | F | 14/04/60 | 43 | Caucasian | N/A | Non | Occasional | N/A | 160.0 | 58.6 |
| 142 | G-F | F | 30/03/43 | 60 | Caucasian | Italy | Non | Occasional | N/A | 165.0 | 75.0 |
| 143 | MFB | F | 14/09/70 | 33 | Caucasian | Australia | Daily | Occasional | Negative | 157.0 | 61.5 |
| 144 | M-V | F | 21/08/67 | 36 | Caucasian | Croatia | Non | Occasional | Negative | 169.0 | 56.8 |
| 145 | B-W | F | 06/03/52 | 51 | Caucasian | Australia | Non | Occasional | N/A | 153.0 | 56.0 |
| 146 | JAK | F | 28/03/84 | 19 | Caucasian | Australia | Daily | Occasional | Negative | 153.0 | 51.9 |
| 147 | P-F | F | 02/04/67 | 36 | Caucasian | Australia | Non | Occasional | Negative | 165.0 | 78.0 |
| 148 | SJW | M | 23/04/71 | 32 | Caucasian | Australia | Daily | Daily | N/A | 187.5 | 91.7 |

| Patient Number | Initials | Sex | DOB | Age at Consent | Ethnicity | Country of Birth | Smoking Status | Alcohol | Pregnancy | Height (cm) | Weight at Baseline (Kg) |
|----------------|----------|-----|----------|----------------|-----------|------------------|----------------|------------|-----------|-------------|-------------------------|
| 149 | D-C | F | 26/05/67 | 36 | Caucasian | Australia | Non | Never | Negative | 165.0 | 79.8 |
| 150 | G-C | M | 05/11/47 | 56 | Caucasian | Australia | Non | Occasional | N/A | 175.0 | 87.0 |
| 151 | S-A | F | 06/12/72 | 31 | Caucasian | Australia | Non | Occasional | Negative | 150.0 | 50.0 |
| 152 | PGB | M | 10/03/52 | 52 | Caucasian | Australia | Non | Daily | N/A | 160.0 | 60.0 |
| 153 | AMG | F | 05/11/35 | 68 | Caucasian | Italy | Non | Never | N/A | 150.0 | 55.3 |
| 154 | P-Q | F | 13/06/49 | 54 | Caucasian | Australia | Daily | Never | N/A | 162.5 | 46.5 |
| 155 | MER | M | 04/12/62 | 41 | Caucasian | Australia | Non | Occasional | N/A | 167.0 | 78.6 |
| 156 | RST | M | 14/03/50 | 54 | Caucasian | Australia | Non | Daily | N/A | 169.0 | 90.5 |
| 157 | C-A | F | 16/12/74 | 29 | Caucasian | Australia | Non | Never | Negative | 140.0 | 43.4 |
| 158 | EWB | M | 08/10/52 | 51 | Caucasian | Australia | Non | Occasional | N/A | 180.0 | 99.5 |
| 159 | D-B | M | 10/04/46 | 57 | Caucasian | Italy | Non | Daily | N/A | 168.0 | 89.8 |
| 160 | A-G | M | 01/02/61 | 43 | Caucasian | Australia | Non | Never | N/A | 181.0 | 75.0 |
| 161 | GRN | M | 21/08/49 | 55 | Caucasian | Australia | Non | Daily | N/A | 179.0 | 81.0 |
| 162 | M-A | F | 11/05/59 | 44 | Caucasian | Australia | Non | Occasional | N/A | 165.0 | 101.2 |

12.1.4 Compliance Data

Table 12.1.4.1: Compliance of Hypertonic Solution and PicoPrep™ Capsules

| Pt No. | HY Bottles dispensed (mg) | HY returned | HY Compliance | # PC dispensed | # PC returned | PC compliance * | Overall Compliance % |
|----------------------|---------------------------|-------------|---------------|----------------|---------------|-----------------|----------------------|
| 107 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 114 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 116 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 117 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 118 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 120 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 122 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 131 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 132 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 134 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 137 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 147 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 153 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 155 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| 159 | 1 (15.564mg) | 0 | 100.0% | 30 | 10 | 100.0% | 100.0% |
| Overall Compliance % | | | | | | | 100.0% |

* PC used per protocol was 20 capsules. Therefore, the return of 10 capsules indicates 100% compliance.

Table 12.1.4.2: Compliance of PicoPrep™ Capsules

| Patient Number | No. capsules dispensed | No. capsules returned* | Overall Compliance % |
|----------------------|------------------------|------------------------|----------------------|
| 101 | 30 | 0 | 100.0% |
| 102 | 30 | 0 | 100.0% |
| 110 | 30 | 0 | 100.0% |
| 111 | 30 | 0 | 100.0% |
| 124 | 30 | 0 | 100.0% |
| 125 | 30 | 0 | 100.0% |
| 126 | 30 | 0 | 100.0% |
| 128 | 30 | 0 | 100.0% |
| 129 | 30 | 0 | 100.0% |
| 135 | 30 | 0 | 100.0% |
| 139 | 30 | 15 | 50.0% |
| 144 | 30 | 15 | 50.0% |
| 150 | 30 | 15 | 50.0% |
| 156 | 30 | 0 | 100.0% |
| 158 | 30 | 0 | 100.0% |
| 162 | 30 | 0 | 100.0% |
| Average Compliance % | | | 91.6% |

* PC used per protocol was 30 capsules. Therefore, the return of 0 capsules indicates 100% compliance.

Table 12.1.4.3: Compliance of Standard PicoPrep™

| Patient Number | Sachets dispensed (mg) | No. sachets returned full | Overall Compliance % |
|----------------------|------------------------|---------------------------|----------------------|
| 104 | 1 (15.567mg) | 0 | 100.0% |
| 105 | 1 (15.567mg) | 0 | 100.0% |
| 109 | 1 (15.567mg) | 0 | 100.0% |
| 112 | 1 (15.567mg) | 0 | 100.0% |
| 130 | 1 (15.567mg) | 0 | 100.0% |
| 133 | 1 (15.567mg) | 0 | 100.0% |
| 140 | 1 (15.567mg) | 0 | 100.0% |
| 141 | 1 (15.567mg) | 0 | 100.0% |
| 142 | 1 (15.567mg) | 0 | 100.0% |
| 143 | 1 (15.567mg) | 0 | 100.0% |
| 145 | 1 (15.567mg) | 0 | 100.0% |
| 149 | 1 (15.567mg) | 0 | 100.0% |
| 152 | 1 (15.567mg) | 0 | 100.0% |
| 154 | 1 (15.567mg) | 0 | 100.0% |
| Average Compliance % | | | 100.0% |

Table 12.1.4.4: Compliance of Standard Glycoprep™

| Patient Number | No. dispensed sachets (g) | No. sachets returned full | Overall Compliance % |
|----------------------|---------------------------|---------------------------|----------------------|
| 103 | 1 (200g) | 0 | 100.0% |
| 106 | 1 (200g) | 0 | 100.0% |
| 108 | 1 (200g) | 0 | 100.0% |
| 113 | 1 (200g) | 0 | 100.0% |
| 115 | 1 (200g) | 0 | 100.0% |
| 119 | 1 (200g) | 0 | 100.0% |
| 123 | 1 (200g) | 0 | 100.0% |
| 127 | 1 (200g) | 0 | 100.0% |
| 136 | 1 (200g) | 0 | 100.0% |
| 146 | 1 (200g) | 0 | 100.0% |
| 148 | 1 (200g) | 0 | 100.0% |
| 151 | 1 (200g) | 0 | 100.0% |
| 157 | 1 (200g) | 0 | 100.0% |
| 161 | 1 (200g) | 0 | 100.0% |
| Average Compliance % | | | 100.0%* |

Overall Compliance for PP subjects

The overall compliance for HYPC, PCA , PS and GS for PP subjects only, was 100.0%, 91.6%, 100.0% and 100.0%, respectively.

12.1.5 Efficacy Response Data

12.1.5.1 Doctor Evaluation

Table 12.1.5.1a Comparison of 'Hypertonic Solution and PicoPrep™ Capsules' and 'PicoPrep™ Capsules' in adequacy of cleansing

| Doctor Evaluation Question | Response | Hypertonic Solution and PicoPrep™ Capsules (n=15) n (%) | PicoPrep™ Capsules (n=15) n (%) | P-value |
|----------------------------|------------|---|---------------------------------------|---------|
| Adequacy of cleansing | Excellent | 5 (33) | 3 (20) | 0.68 |
| | Good | 5 (33) | 5 (33) | NS |
| | Fair | 2 (13) | 5 (33) | 0.38 |
| | Poor | 3 (20) | 1 (7) | NS |
| | Inadequate | 0 (0) | 1 (7) | NS |
| Missing data | | 0 (0) | 0 (0) | |

Table 12.1.5.1b Comparison of 'Hypertonic Solution and PicoPrep™ capsules' and 'PicoPrep™ Capsules' rating in specific bowel areas

| Bowel Preparation | Mean Rating for Specific Bowel Areas (out of 10) | | | |
|--|--|------------------|--------|----------------|
| | Rectum | Transverse Colon | Caecum | Terminal Ileum |
| Hypertonic Solution and PicoPrep™ Capsules | 8.60 | 8.60 | 6.33 | 8.13 |
| PicoPrep™ Capsules | 7.00 | 6.86 | 5.93 | 8.42 |
| p-value | 0.14 | 0.03 | 0.03 | 0.57 |

Table 12.1.5.1c Comparison of 'Hypertonic Solution and PicoPrep™ Capsules' with 'Standard PicoPrep™'

| Doctor Evaluation Question | Response | Hypertonic Solution and PicoPrep™ Capsules (n=15) n (%) | Standard PicoPrep™ (n=15) n (%) | P-value |
|----------------------------|------------|---|---------------------------------------|---------|
| Adequacy of cleansing | Excellent | 5 (33) | 5 (33) | NS |
| | Good | 5 (33) | 4 (27) | NS |
| | Fair | 2 (13) | 3 (20) | NS |
| | Poor | 3 (20) | 1 (7) | 0.59 |
| | Inadequate | 0 (0) | 0 (0) | NS |
| Missing data | | 0 (0) | 2 (13) | |

Table 12.1.5.1d Comparison of 'Hypertonic Solution and PicoPrep™ capsules' with 'Standard PicoPrep™' rating in specific bowel areas.

| Bowel Preparation | Mean Rating for Specific Bowel Areas (out of 10) | | | |
|--|--|------------------|--------|----------------|
| | Rectum | Transverse Colon | Caecum | Terminal Ileum |
| Hypertonic Solution and PicoPrep™ Capsules | 8.60 | 8.60 | 6.33 | 8.13 |
| Standard PicoPrep™ | 8.47 | 8.27 | 7.80 | 8.60 |
| p-value | 0.32 | 0.82 | 0.10 | 0.37 |

Table 12.1.5.1e Comparison of 'Hypertonic Solution and PicoPrep™ capsules' with 'Standard Glycoprep™'

| Doctor Evaluation Question | Response | Hypertonic Solution and PicoPrep™ Capsules (n=15) n (%) | Standard Glycoprep™ (n=14) n (%) | P-value |
|----------------------------|------------|---|--|---------|
| Adequacy of cleansing | Excellent | 5 (33) | 3 (21) | 0.68 |
| | Good | 5 (33) | 3 (21) | 0.68 |
| | Fair | 2 (13) | 5 (36) | 0.21 |
| | Poor | 3 (20) | 2 (14) | NS |
| | Inadequate | 0 (0) | 0 (0) | NS |
| Missing data | | 0 (0) | 1 (7) | |

Table 12.1.5.1f Comparison of 'Hypertonic Solution and PicoPrep™ capsules' with 'Standard Glycoprep™' rating in specific bowel areas

| Bowel Preparation | Mean Rating for Specific Bowel Areas (out of 10) | | | |
|--|--|------------------|--------|----------------|
| | Rectum | Transverse Colon | Caecum | Terminal Ileum |
| Hypertonic Solution and PicoPrep™ Capsules | 8.60 | 8.60 | 6.33 | 8.13 |
| Standard Glycoprep™ | 7.21 | 7.07 | 6.36 | 7.86 |
| p-value | 0.14 | 0.14 | 0.95 | 0.74 |

Table 12.1.5.1g Comparison of 'PicoPrep™ Capsules' and 'Standard PicoPrep™'

| Doctor Evaluation Question | Response | PicoPrep™ Capsules (n=15) n (%) | Standard PicoPrep™ (n=15) n (%) | P-value |
|-----------------------------------|-----------------|--|--|----------------|
| Adequacy of cleansing | Excellent | 3 (20) | 3 (21) | 0.68 |
| | Good | 5 (33) | 3 (21) | NS |
| | Fair | 5 (33) | 5 (36) | 0.68 |
| | Poor | 1 (7) | 2 (14) | NS |
| | Inadequate | 1 (7) | 0 (0) | NS |
| Missing data | | 0 (0) | 1 (7) | |

Table 12.1.5.1h Comparison of 'PicoPrep™ Capsules' and 'Standard PicoPrep™' rating in specific bowel areas

| Bowel Preparation | Mean Rating for Specific Bowel Areas (out of 10) | | | |
|--------------------------|---|-------------------------|---------------|-----------------------|
| | Rectum | Transverse Colon | Caecum | Terminal Ileum |
| PicoPrep™ Capsules | 7.00 | 6.86 | 5.93 | 8.42 |
| Standard PicoPrep™ | 8.47 | 8.27 | 7.80 | 8.60 |
| p-value | 0.06 | 0.08 | 0.03 | 0.83 |

Table 12.1.5.1i Comparison of 'PicoPrep™ Capsules' and 'Standard Glycoprep™'

| Doctor Evaluation Question | Response | PicoPrep™ Capsules (n=15) n (%) | Standard Glycoprep™ (n=14) n (%) | P-value |
|-----------------------------------|-----------------|--|---|----------------|
| Adequacy of cleansing | Excellent | 3 (20) | 5 (33) | 0.68 |
| | Good | 5 (33) | 4 (27) | 0.68 |
| | Fair | 5 (33) | 3 (20) | NS |
| | Poor | 1 (7) | 1 (7) | NS |
| | Inadequate | 1 (7) | 0 (0) | NS |
| Missing data | | 0 (0) | 2 (13) | |

Table 12.1.5.1j Comparison of 'PicoPrep™ capsules' and 'Standard Glycoprep™' rating in specific bowel areas

| Bowel Preparation | Mean Rating for Specific Bowel Areas (out of 10) | | | |
|--------------------------|---|-------------------------|---------------|-----------------------|
| | Rectum | Transverse Colon | Caecum | Terminal Ileum |
| PicoPrep™ Capsules | 7.00 | 6.86 | 5.93 | 8.42 |
| Standard Glycoprep™ | 7.21 | 7.07 | 6.36 | 7.86 |
| p-value | 0.46 | 0.82 | 0.49 | 0.55 |

12.1.6 Adverse Events

A. Comparison of 'GlycoprepTM' with 'Hypertonic Solution and PicoPrepTM Capsules'

| Adverse Events | GS (n = 14) n (%) | HYPC (n = 15) n (%) | P values |
|--|----------------------------------|------------------------------------|-----------------|
| Moderate or severe adverse events | | | |
| Headache | 1 (7.14) | 4 (26.66) | 0.17 |
| Vomiting | 1 (7.14) | 0 (0.00) | - |
| Bloating | 1 (7.14) | 0 (0.00) | - |
| Mild adverse events | | | |
| Headache | 4 (28.6) | 4 (26.66) | - |
| Vomiting | 1 (7.14) | 0 (0.00) | - |
| Faint/Light headed | 1 (7.14) | 1 (6.66) | - |
| Total number of subjects reporting adverse events | 8 (57.14) | 7 (46.66) | |

B. Comparison of 'GlycoprepTM' with 'PicoPrepTM Capsules'

| Adverse Events | GS (n = 14) n (%) | PCA (n = 16) n (%) | P value |
|--|----------------------------------|-----------------------------------|----------------|
| Moderate or severe adverse events | | | |
| Headache | 1 (7.14) | 2 (12.50) | - |
| Nausea | 0 (0.00) | 1 (6.25) | - |
| Vomiting | 1 (7.14) | 2 (12.5) | - |
| Bloating | 1 (7.14) | 0 (0.00) | - |
| Faint/Light headed | 0 (0.00) | 1 (6.25) | - |
| Anal irritation | 0 (0.00) | 1 (6.25) | - |
| Mild adverse events | | | |
| Headache | 4 (28.57) | 1 (6.25) | 0.33 |
| Vomiting | 1 (7.14) | - | - |
| Faint/Light headed | 1 (7.14) | - | - |
| Total number of subjects reporting adverse events | 8 (57.14) | 8 (50.00) | |

C. Comparison of 'Hypertonic Solution and PicoPrep™ Capsules' and 'PicoPrep™ Capsules'

| Adverse Events | HYPC (n = 15) n (%) | PCA (n = 16) n (%) | P value |
|--|------------------------------------|-----------------------------------|--------------------|
| Moderate or severe adverse events | | | |
| Headache | 4 (26.66) | 2 (12.5) | 0.39 |
| Nausea | 0 (0.00) | 1 (6.25) | - |
| Vomiting | 0 (0.00) | 2 (13) | - |
| Faint/Light headed | 0 (0.00) | 1 (6.25) | - |
| Anal irritation | 0 (0.00) | 1 (6.25) | - |
| Mild adverse events | | | |
| Headache | 4 (26.66) | 1 (6.25) | 0.16 |
| Faint/Light headed | 1 (6.66) | 0 (0.00) | - |
| Total number of subjects reporting adverse events | 7 (46.66) | 8 (50.00) | |

D. Comparison of 'PicoPrep™ Sachets' with 'Hypertonic Solution and PicoPrep™ Capsules'

| Adverse Events | PS (n = 14) n (%) | HYPC (n = 15) n (%) | P value |
|--|----------------------------------|------------------------------------|--------------------|
| Moderate or severe adverse events | | | |
| Headache | 1 (7.14) | 4 (26.66) | 0.32 |
| Vomiting | 1 (7.14) | 0 (0.00) | - |
| Faint/Light headed | 2 (15.38) | 0 (0.00) | 0.48 |
| Hyperventilating | 1 (7.14) | 0 (0.00) | - |
| Tremor | 1 (7.14) | 0 (0.00) | - |
| Mild adverse events | | | |
| Headache | 4 (28.57) | 4 (26.66) | - |
| Faint/Light headed | 0 (0.00) | 1 (6.66) | - |
| Bloating | 1 (7.14) | 0 (0.00) | - |
| Dry mouth | 1 (7.14) | 0 (0.00) | - |
| Total number of subjects reporting adverse events | 7 (41.17) | 7 (46.66) | |

E. Comparison of 'PicoPrep™ Sachets' with 'PicoPrep™ Capsules'

| Adverse Events | PS (n = 14) n (%) | PCA (n = 16) n (%) | P value |
|--|----------------------------------|-----------------------------------|----------------|
| Moderate or severe adverse events | | | |
| Headache | 1 (7.14) | 2 (12.50) | - |
| Nausea | 0 (0.00) | 1 (6.25) | - |
| Vomiting | 1 (7.14) | 2 (12.50) | - |
| Faint/Light headed | 2 (13.28) | 1 (6.25) | - |
| Hyperventilating | 1 (7.14) | 0 (0.00) | - |
| Tremor | 1 (7.14) | | - |
| Anal irritation | 0 (0.00) | 1 (6.25) | - |
| Mild adverse events | | | |
| Headache | 4 (28.57) | 1 (6.25) | 0.17 |
| Bloating | 1 (7.14) | | - |
| Dry mouth | 1 (7.14) | | - |
| Total number of subjects reporting adverse events | 7 (50.00) | 8 (50.00) | |

12.1.7 List of Drug Batches per Subject

| Patient Number | Preparation Dispensed at Visit 1 | Batch Nos. |
|----------------|--|-----------------------|
| 101 | PicoPrep™ Capsules | B0136N, B11181 |
| 102 | PicoPrep™ Capsules | B0136N, B11181 |
| 103 | Standard Glycoprep™ | B30112 |
| 104 | Standard PicoPrep™ | B30531 |
| 105 | Standard PicoPrep™ | B30531 |
| 106 | Standard Glycoprep™ | B30112 |
| 107 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181 |
| 108 | Standard Glycoprep™ | B30112 |
| 109 | Standard PicoPrep™ | B30531 |
| 110 | PicoPrep™ Capsules | B0136N, B11181 |
| 111 | PicoPrep™ Capsules | B0136N, B11181 |
| 112 | Standard PicoPrep™ | B30531 |
| 113 | Standard Glycoprep™ | B30112 |
| 114 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181 |
| 115 | Standard Glycoprep™ | B30112 |
| 116 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 117 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 118 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181 |
| 119 | Standard Glycoprep™ | B30112 |
| 120 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181 |
| 121 | Standard Glycoprep™ | B30112 |
| 122 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181 |
| 123 | Standard Glycoprep™ | B30112 |
| 124 | PicoPrep™ Capsules | B0136N, B11181 |
| 125 | PicoPrep™ Capsules | B0136N, B11181 |
| 126 | PicoPrep™ Capsules | B0136N, B11181 |
| 127 | Standard Glycoprep™ | B30112 |
| 128 | PicoPrep™ Capsules | B0136N, B11181 |
| 129 | PicoPrep™ Capsules | B0136N, B11181 |
| 130 | Standard PicoPrep™ | B30531 |
| 131 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 132 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 133 | Standard PicoPrep™ | B30531 |
| 134 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 135 | PicoPrep™ Capsules | B0136N, B11181 |

| Patient Number | Preparation Dispensed at Visit 1 | Batch Nos. |
|----------------|--|-----------------------|
| 136 | Standard Glycoprep™ | B30112 |
| 137 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 138 | PicoPrep™ Capsules | B0136N, B11181 |
| 139 | PicoPrep™ Capsules | B0136N, B11181 |
| 140 | Standard PicoPrep™ | B30531 |
| 141 | Standard PicoPrep™ | B30531 |
| 142 | Standard PicoPrep™ | B30531 |
| 143 | Standard PicoPrep™ | B30531 |
| 144 | PicoPrep™ Capsules | B0136N, B11181 |
| 145 | Standard PicoPrep™ | B30531 |
| 146 | Standard Glycoprep™ | B30112 |
| 147 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 148 | Standard Glycoprep™ | B30112 |
| 149 | Standard PicoPrep™ | B30531 |
| 150 | PicoPrep™ Capsules | B0136N, B11181 |
| 151 | Standard Glycoprep™ | B30112 |
| 152 | Standard PicoPrep™ | B30531 |
| 153 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 154 | Standard PicoPrep™ | B30531 |
| 155 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 156 | PicoPrep™ Capsules | B0136N, B11181 |
| 157 | Standard Glycoprep™ | B30112 |
| 158 | PicoPrep™ Capsules | B0136N, B11181 |
| 159 | Hypertonic Solution and PicoPrep™ Capsules | B0136N, B11181, C0804 |
| 160 | Standard Glycoprep™ | B30112 |
| 161 | Standard Glycoprep™ | B30899 |
| 162 | PicoPrep™ Capsules | B0136N, B11181 |

12.1.8 Individual Subject Laboratory Results

Table 12.1.8.1: Full Blood Count Values per Subject

| Patient No. | Haemoglobin (120 - 160 g/L) | | Haematocrit (0.370 - 0.470) | | Erythrocytes (RBC) (3.74 - 5.16 *10 ¹² /L) | | Leucocytes (WBC) (4.0 - 11.0 *10 ⁹ /L) | | Platelets (PTLC) (150 - 400 *10 ⁹ /L) | |
|-------------|--------------------------------|---------|--------------------------------|---------|--|---------|--|---------|---|---------|
| | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 101 | 138 | 141 | 0.426 | 0.438 | 4.65 | 4.77 | 7.7 | 6.6 | 337 | 337 |
| 102 | 148 | 144 | 0.435 | 0.419 | 4.57 | 4.41 | 9.2 | 7.6 | 284 | 285 |
| 103 | 160 | 166* | 0.447 | 0.473* | 4.76 | 5.01 | 5.0 | 5.0 | 206 | 239 |
| 104 | 162 | 160 | 0.464 | 0.458 | 5.15 | 5.19 | 8.1 | 6.5 | 184 | 158 |
| 105 | 139 | 143 | 0.409 | 0.416 | 4.30 | 4.49 | 4.1 | 4.8 | 211 | 224 |
| 106 | 134 | 133 | 0.41 | 0.41 | 4.80 | 4.82 | 7.0 | 7.3 | 306 | 266 |
| 107 | 135 | 142 | 0.421 | 0.437 | 4.40 | 4.57 | 5.5 | 5.0 | 310 | 303 |
| 108 | 157 | 140 | 0.458 | 0.405 | 5.11 | 4.58 | 3.6* | 4.3 | 151 | 132* |
| 109 | 133 | 1389 | 0.407 | 0.410 | 4.36 | 4.44 | 6.1 | 4.8 | 278 | 210 |
| 110 | 174 | 164 | 0.489 | 0.471 | 5.55 | 5.35 | 5.3 | 4.7 | 119* | 116* |
| 111 | 131 | 133 | 0.391 | 0.399 | 4.33 | 4.48 | 4.5 | 5.5 | 269 | 200 |
| 112 | 152 | 150 | 0.443 | 0.437 | 4.98 | 4.91 | 10.0 | 7.7 | 304 | 274 |
| 113 | 160 | 160 | 0.450 | 0.452 | 5.38 | 5.34 | 7.8 | 7.8 | 232 | 216 |
| 114 | 160 | 155 | 0.450 | 0.437 | 4.82 | 4.66 | 4.5 | 3.7* | 202 | 200 |
| 115 | 158 | 155 | 0.484 | 0.465 | 5.40 | 5.25 | 5.7 | 5.2 | 226 | 186 |
| 116 | 149 | 152 | 0.446 | 0.453 | 4.89 | 5.02 | 6.5 | 4.4 | 242 | 229 |
| 117 | 143 | 140 | 0.429 | 0.418 | 4.49 | 4.42 | 7.9 | 6.5 | 265 | 221 |
| 118 | 144 | 141 | 0.444 | 0.429 | 4.94 | 4.87 | 5.1 | 5.3 | 126 | 187 |
| 119 | 152 | 145 | 0.447 | 0.431 | 5.28 | 5.09 | 4.8 | 8.0 | 220 | 215 |
| 120 | 119 | 122 | 0.365 | 0.377 | 4.34 | 4.46 | 5.3 | 4.3 | 429 | 385 |
| 121 | 133 | N/A | 0.402 | N/A | 4.12 | N/A | 7.2 | N/A | 316 | N/A |
| 122 | 134 | 145 | 0.396 | 0.437 | 4.37 | 4.38 | 6.3 | 5.1 | 215 | 208 |
| 123 | 125 | 119* | 0.381 | 0.365* | 4.06 | 3.86 | 13.1* | 8.5 | 451* | 399 |
| 124 | 112* | 118* | 0.358* | 0.371 | 5.88* | 6.14* | 9.1 | 9.3 | 366 | 347 |
| 125 | 166 | 169 | 0.491 | 0.494 | 5.45 | 5.53 | 8.6 | 6.2 | 200 | 184 |
| 126 | 131 | 136 | 0.396 | 0.410 | 4.32 | 4.51 | 6.5 | 7.0 | 196 | 172 |
| 127 | 133 | 133 | 0.426 | 0.419 | 4.74 | 4.75 | 9.8 | 9.9 | 255 | 212 |
| 128 | 144 | 145 | 0.421 | 0.421 | 4.55 | 4.52 | 9.8 | 7.1 | 226 | 220 |
| 129 | 151 | 143 | 0.442 | 0.420 | 4.80 | 4.55 | 5.1 | 4.0 | 219 | 185 |
| 130 | 143 | 129 | 0.425 | 0.387 | 4.71 | 4.29 | 4.7 | 5.0 | 307 | 258 |
| 131 | 153 | 152 | 0.476* | 0.459 | 5.96 | 5.79* | 7.7 | 6.6 | 256 | 239 |
| 132 | 140 | 138 | 0.412 | 0.417 | 4.35 | 4.36 | 4.9 | 4.3 | 211 | 216 |
| 133 | 120 | 125 | 0.371 | 0.397 | 3.97 | 4.29 | 5.7 | 5.3 | 190 | 172 |

| | Haemoglobin (120 - 160 g/L) | | Haematocrit (0.370 - 0.470) | | Erythrocytes (RBC) (3.74 - 5.16 *10 ¹² /L) | | Leucocytes (WBC) (4.0 - 11.0 *10 ⁹ /L) | | Platelets (PTLC) (150 - 400 *10 ⁹ /L) | |
|-------------|--------------------------------|---------|--------------------------------|---------|--|---------|--|---------|---|---------|
| Patient No. | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 134 | 150 | 152 | 0.455 | 0.452 | 4.81 | 4.89 | 5.7 | 4.3 | 222 | 218 |
| 135 | 157 | 158 | 0.468 | 0.477 | 5.22 | 5.20 | 5.7 | 6.2 | 257 | 254 |
| 136 | 132 | 131 | 0.395 | 0.398 | 4.45 | 4.42 | 6.7 | 6.4 | 259 | 229 |
| 137 | 156 | 159 | 0.466 | 0.475* | 4.59 | 4.70 | 6.1 | 5.4 | 198 | 190 |
| 138 | 135 | 133 | 0.410 | 0.393 | 4.28 | 4.19 | 4.1 | 3.9* | 192 | 177 |
| 139 | 138 | 139 | 0.426 | 0.428 | 4.48 | 4.54 | 3.9* | 3.9* | 304 | 290 |
| 140 | 131 | 132 | 0.409 | 0.414 | 4.12 | 4.15 | 5.3 | 5.1 | 270 | 254 |
| 141 | 128 | 130 | 0.394 | 0.396 | 4.44 | 4.49 | 3.7* | 3.5* | 254 | 242 |
| 142 | 129 | 121 | 0.413 | 0.395 | 4.90 | 4.66 | 6.9 | 5.1 | 251 | 215 |
| 143 | 131 | 135 | 0.411 | 0.416 | 4.48 | 4.54 | 3.6* | 3.8* | 276 | 265 |
| 144 | 130 | 141 | 0.403 | 0.422 | 4.47 | 4.77 | 7.3 | 4.9 | 225 | 212 |
| 145 | 128 | 124 | 0.382 | 0.343* | 4.02 | 3.89 | 5.2 | 6.2 | 227 | 191 |
| 146 | 143 | 139 | 0.439 | 0.414 | 4.41 | 4.22 | 8.6 | 13.1* | 308 | 292 |
| 147 | 128 | 135 | 0.391 | 0.412 | 4.18 | 4.44 | 6.2 | 5.5 | 235 | 227 |
| 148 | 169 | 161 | 0.522* | 0.496 | 5.51 | 5.23 | 6.3 | 6.2 | 163 | 155 |
| 149 | 129 | 136 | 0.388 | 0.410 | 4.41 | 4.62 | 6.8 | 6.6 | 329 | 324 |
| 150 | 165 | 165 | 0.482 | 0.498 | 5.42 | 5.46 | 4.5 | 5.4 | N/A | N/A |
| 151 | 131 | 129 | 0.411 | 0.394 | 4.40 | 4.27 | 4.1 | 4.6 | 262 | 231 |
| 152 | 154 | 147 | 0.470 | 0.440 | 4.92 | 4.67 | 6.3 | 6.1 | 343 | 340 |
| 153 | 136 | 144 | 0.432 | 0.469 | 4.89 | 5.23* | 8.6 | 5.9 | 292 | 307 |
| 154 | 128 | 125 | 0.398 | 0.409 | 4.09 | 4.02 | 6.2 | 4.9 | 287 | 256 |
| 155 | 168 | 161 | 0.500 | 0.477 | 5.62* | 5.37 | 5.8 | 5.9 | 214 | 197 |
| 156 | 146 | 157 | 0.434 | 0.464 | 4.88 | 5.30 | 7.7 | 8.8 | 303 | 262 |
| 157 | 127 | 133 | 0.382 | 0.396 | 4.30 | 4.48 | 8.0 | 8.2 | 238 | 223 |
| 158 | 156 | 155 | 0.463 | 0.449 | 5.07 | 4.94 | 5.8 | 4.6 | 198 | 157 |
| 159 | 156 | 159 | N/A | 0.459 | N/A | 4.85 | 8.0 | 6.5 | N/A | 149 |
| 160 | 152 | N/A | 0.466 | N/A | 5.72 | N/A | 7.5 | N/A | 219 | N/A |
| 161 | 140 | 135 | 0.447 | 0.434 | 5.53 | 5.45 | 4.8 | 4.5 | 328 | 313 |
| 162 | 144 | 150 | 0.435 | 0.459 | 4.63 | 4.88 | 6.4 | 3.7 | 225 | 187 |

* Out of normal range. Not clinically significant

Table 12.1.8.2: Biochemistry Values per Subject

| Patient No. | Sodium (135 – 150 mmol/L) | | Potassium (3.25 – 5.0 mmol/L) | | Chloride (95 – 110 mmol/L) | | Urea (3.6 – 9.3 mmol/L) | | Creatinine (0.06 – 0.12 mmol/L) | | Calcium (2.10–2.65 mmol/L) | | Phosphate (0.80-1.50 mmol/L) | |
|-------------|------------------------------|---------|----------------------------------|---------|-------------------------------|---------|----------------------------|---------|------------------------------------|---------|-------------------------------|---------|---------------------------------|---------|
| | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 101 | 140 | 141 | 4.7 | 4.6 | 101 | 99 | 5.9 | 6.1 | 0.086 | 0.091 | 2.27 | 2.26 | 1.01 | 1.06 |
| 102 | 142 | 143 | 3.6 | 4.1 | 104 | 105 | 5.1 | 4.0 | 0.080 | 0.071 | 2.35 | 2.12 | 1.12 | 0.91 |
| 103 | 139 | 140 | 3.9 | 4.7 | 102 | 100 | 7.7 | 5.3 | 0.082 | 0.078 | 2.24 | 2.20 | 0.93 | 1.25 |
| 104 | 139 | 137 | 4.5 | 4.2 | 102 | 101 | 7.0 | 4.9 | 0.110 | 0.099 | 2.43 | 2.32 | 1.09 | 0.97 |
| 105 | 137 | 136 | 4.2 | 4.0 | 103 | 100 | 2.8* | 3.4* | 0.058* | 0.065 | 2.34 | 2.31 | 1.16 | 1.15 |
| 106 | 139 | 140 | 3.7 | 3.8 | 103 | 102 | 2.5 | 2.6 | 0.080 | 0.080 | 2.47 | 2.43 | 1.12 | 1.01 |
| 107 | 141 | 142 | 4.1 | 3.8 | 103 | 104 | 6.4 | 5.7 | 0.056* | 0.056* | 2.36 | 2.31 | 1.06 | 1.03 |
| 108 | 139 | 142 | 4.0 | 4.3 | 102 | 101 | 5.8 | 3.7 | 0.086 | 0.080 | 2.53 | 2.32 | 0.95 | 0.82 |
| 109 | 141 | 137 | 4.7 | 4.5 | 101 | 102 | 6.1 | 4.4 | 0.069 | 0.066 | 2.50 | 2.44 | 1.25 | 1.11 |
| 110 | 138 | 141 | 4.4 | 4.2 | 102 | 104 | 5.7 | 4.6 | 0.089 | 0.074 | 2.33 | 2.14 | 0.82 | 0.80 |
| 111 | 138 | 141 | 4.2 | 3.8 | 105 | 106 | 5.2 | 3.2* | 0.069 | 0.066 | 2.39 | 2.34 | 1.26 | 1.18 |
| 112 | 139 | 141 | 4.5 | 4.7 | 102 | 104 | 5.5 | 5.3 | 0.080 | 0.074 | 2.43 | 2.19 | 1.38 | 1.06 |
| 113 | 141 | 140 | 4.1 | 4.2 | 102 | 100 | 4.7 | 5.5 | 0.089 | 0.084 | 2.39 | 2.30 | 1.01 | 1.04 |
| 114 | 138 | 141 | 4.6 | 4.2 | 101 | 103 | 6.3 | 4.1 | 0.082 | 0.067 | 2.55 | 2.45 | 1.22 | 1.12 |
| 115 | 140 | 143 | 4.8 | 4.1 | 105 | 109 | 7.4 | 6.6 | 0.109 | 0.105 | 2.26 | 2.24 | 1.33 | 1.20 |
| 116 | 144 | 142 | 3.6 | 3.5 | 106 | 106 | 4.1 | 2.0* | 0.055* | 0.051* | 2.34 | 2.34 | 1.25 | 1.00 |
| 117 | 140 | 138 | 3.9 | 3.6 | 101 | 104 | 4.7 | 3.6 | 0.059* | 0.043* | 2.21 | 2.00* | 1.13 | 1.05 |
| 118 | 142 | 144 | 4.3 | 3.8 | 106 | 106 | 7.5 | 6.6 | 0.065 | 0.061* | 2.47 | 2.40 | 1.05 | 1.02 |
| 119 | 143 | 139 | 4.2 | 3.7 | 106 | 102 | 7.6 | 5.1 | 0.074 | 0.071 | 2.41 | 2.29 | 1.17 | 1.10 |
| 120 | 137 | 138 | 4.5 | 4.4 | 107 | 106 | 3.4* | 2.5* | 0.064 | 0.065 | 2.27 | 2.13 | 1.06 | 1.02 |
| 121 | 144 | N/A | 4.1 | N/A | 105 | N/A | 5.1 | N/A | 0.054* | N/A | 2.38 | N/A | 1.47 | N/A |
| 122 | 140 | 140 | 4.1 | 4.2 | 102 | 100 | 6.3 | 4.2 | 0.074 | 0.079 | 2.35 | 2.24 | 1.21 | 1.08 |

| Patient No. | Sodium (135 – 150 mmol/L) | | Potassium (3.25 – 5.0 mmol/L) | | Chloride (95 – 110 mmol/L) | | Urea (3.6 – 9.3 mmol/L) | | Creatinine (0.06 – 0.12 mmol/L) | | Calcium (2.10–2.65 mmol/L) | | Phosphate (0.80-1.50 mmol/L) | |
|-------------|------------------------------|---------|----------------------------------|---------|-------------------------------|---------|----------------------------|---------|------------------------------------|---------|-------------------------------|---------|---------------------------------|---------|
| | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 123 | 140 | 137 | 4.4 | 4.6 | 105 | 104 | 3.8 | 3.8 | 0.056* | 0.049* | 2.32 | 2.30 | 1.36 | 1.33 |
| 124 | 139 | 141 | 4.0 | 4.7 | 104 | 105 | 5.4 | 4.8 | 0.066 | 0.073 | 2.32 | 2.31 | 1.07 | 1.08 |
| 125 | 141 | 140 | 4.2 | 4.0 | 108 | 105 | 8.7 | 5.4 | 0.098 | 0.088 | 2.41 | 2.40 | 1.02 | 0.91 |
| 126 | 140 | 143 | 4.1 | 4.5 | 105 | 106 | 5.4 | 4.4 | 0.058* | 0.066 | 2.38 | 2.34 | 1.29 | 1.04 |
| 127 | 138 | 142 | 4.5 | 3.7 | 103 | 107 | 5.9 | 3.7 | 0.062 | 0.062 | 2.30 | 2.40 | 1.19 | 1.02 |
| 128 | 141 | 138 | 4.3 | 4.5 | 106 | 101 | 5.2 | 3.4* | 0.075 | 0.085 | 2.28 | 2.28 | 0.82 | 0.97 |
| 129 | 138 | 139 | 4.5 | 4.4 | 103 | 106 | 5.3 | 3.8 | 0.079 | 0.076 | 2.43 | 2.27 | 1.11 | 0.80 |
| 130 | 139 | 140 | 4.4 | 4.2 | 104 | 106 | 6.3 | 5.1 | 0.077 | 0.071 | 2.41 | 2.31 | 1.24 | 1.20 |
| 131 | 141 | 138 | 4.3 | 4.0 | 101 | 100 | 7.4 | 4.7 | 0.088 | 0.083 | 2.28 | 2.21 | 1.01 | 0.98 |
| 132 | 140 | 141 | 3.8 | 3.9 | 105 | 107 | 7.8 | 4.8 | 0.094 | 0.079 | 2.15 | 2.03* | 0.88 | 0.98 |
| 133 | 141 | 140 | 4.4 | 4.0 | 105 | 102 | 5.0 | 4.7 | 0.058* | 0.071 | 2.37 | 2.32 | 1.18 | 1.11 |
| 134 | 140 | 139 | 3.6 | 4.2 | 102 | 104 | 8.0 | 5.0 | 0.080 | 0.078 | 2.37 | 2.24 | 1.16 | 1.23 |
| 135 | 138 | 141 | 4.4 | 3.6 | 103 | 102 | 6.7 | 6.0 | 0.082 | 0.092 | 2.49 | 2.38 | 0.90 | 0.88 |
| 136 | 141 | 139 | 4.1 | 3.9 | 104 | 103 | 5.9 | 3.5 | 0.073 | 0.069 | 2.36 | 2.36 | 1.25 | 1.21 |
| 137 | 142 | 139 | 3.9 | 4.2 | 106 | 106 | 5.1 | 2.6* | 0.095 | 0.093 | 2.44 | 2.37 | 0.77* | 1.00 |
| 138 | 144 | 138 | 4.0 | 3.7 | 103 | 100 | 7.0 | 4.5 | 0.103 | 0.066 | 2.40 | 2.39 | 1.26 | 1.34 |
| 139 | 143 | 141 | 4.2 | 3.6 | 110 | 107 | 7.2 | 6.1 | 0.053* | 0.059* | 2.32 | 2.32 | 1.21 | 1.00 |
| 140 | 141 | 144 | 4.2 | 4.2 | 108 | 106 | 6.6 | 4.3 | 0.066 | 0.074 | 2.39 | 2.30 | 1.07 | 1.16 |
| 141 | 140 | 142 | 4.7 | 3.7 | 102 | 102 | 5.3 | 3.8 | 0.083 | 0.082 | 2.58 | 2.40 | 1.32 | 1.25 |
| 142 | 141 | 144 | 4.3 | 4.2 | 106 | 105 | 5.1 | 4.2 | 0.072 | 0.070 | 2.49 | 2.34 | 1.36 | 1.08 |
| 143 | 142 | 142 | 4.1 | 4.3 | 104 | 104 | 3.3* | 2.7* | 0.066 | 0.059* | 2.32 | 2.20 | 1.30 | 1.19 |
| 144 | 140 | 136 | 3.9 | 3.5 | 101 | 99 | 4.8 | 2.9* | 0.056* | 0.056* | 2.25 | 2.29 | 1.19 | 1.30 |
| 145 | 137 | 121* | 3.5 | 3.3* | 98 | 85* | 2.6* | 2.9* | 0.055* | 0.040* | 2.32 | 2.13 | 1.12 | 0.88 |
| 146 | 143 | 143 | 4.2 | 4.2 | 103 | 104 | 3.9 | 3.9 | 0.056* | 0.049* | 2.41 | 2.26 | 1.15 | 1.22 |
| 147 | 140 | 139 | 4.5 | 4.4 | 106 | 105 | 5.4 | 2.3* | 0.069 | 0.071 | 2.35 | 2.15 | 1.15 | 1.10 |

| Patient No. | Sodium (135 – 150 mmol/L) | | Potassium (3.25 – 5.0 mmol/L) | | Chloride (95 – 110 mmol/L) | | Urea (3.6 – 9.3 mmol/L) | | Creatinine (0.06 – 0.12 mmol/L) | | Calcium (2.10–2.65 mmol/L) | | Phosphate (0.80-1.50 mmol/L) | |
|-------------|------------------------------|---------|----------------------------------|---------|-------------------------------|---------|----------------------------|---------|------------------------------------|---------|-------------------------------|---------|---------------------------------|---------|
| | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 148 | 137 | 141 | 3.9 | 4.4 | 102 | 102 | 2.8* | 2.7* | 0.086 | 0.084 | 2.34 | 2.29 | 0.89 | 1.04 |
| 149 | 138 | 140 | 3.7 | 3.2* | 99 | 101 | 3.8 | 2.9* | 0.042* | 0.052* | 2.28 | 2.29 | 0.80 | 1.15 |
| 150 | 140 | 141 | 4.3 | 4.2 | 103 | 103 | 5.2 | 3.8 | 0.079 | 0.084 | 2.24 | 2.25 | 1.09 | 1.04 |
| 151 | 145 | 140 | 4.7 | 3.4 | 105 | 104 | 5.7 | 4.1 | 0.054* | 0.053* | 2.41 | 2.20 | 1.21 | 1.16 |
| 152 | 140 | 139 | 4.6 | 4.4 | 101 | 104 | 5.7 | 3.7 | 0.081 | 0.079 | 2.36 | 2.21 | 1.13 | 1.07 |
| 153 | 144 | 140 | 4.0 | 4.1 | 105 | 104 | 4.5 | 3.8 | 0.067 | 0.066 | 2.48 | 2.46 | 1.33 | 1.19 |
| 154 | 141 | 145 | 4.3 | 4.0 | 104 | 109 | 4.6 | 3.8 | 0.061 | 0.054* | 2.31 | 2.29 | 1.13 | 0.86 |
| 155 | 138 | 140 | 4.4 | 4.1 | 100 | 102 | 5.1 | 4.7 | 0.099 | 0.095 | 2.35 | 2.34 | 0.94 | 0.92 |
| 156 | 138 | 139 | 4.1 | 3.8 | 102 | 100 | 6.1 | 6.5 | 0.093 | 0.099 | 2.41 | 2.28 | 1.15 | 1.05 |
| 157 | 140 | 139 | 3.8 | 4.5 | 105 | 102 | 4.4 | 6.6 | 0.068 | 0.061 | 2.46 | 2.27 | 1.10 | 1.17 |
| 158 | 139 | 141 | 4.3 | 4.1 | 102 | 106 | 8.9 | 6.5 | 0.098 | 0.048 | 2.34 | 2.36 | 1.10 | 1.19 |
| 159 | 121* | 143 | N/A | 4.0 | 96 | 104 | 6.9 | 6.3 | 0.101 | 0.084 | 1.54* | 2.21 | 1.32 | N/A |
| 160 | 137 | N/A | 3.9 | N/A | 103 | N/A | 6.0 | N/A | 0.088 | N/A | 2.30 | N/A | 1.02 | N/A |
| 161 | 142 | 138 | 4.4 | 4.4 | 105 | 100 | 7.5 | 5.1 | 0.115 | 0.109 | 2.44 | 2.31 | 0.71* | 0.94 |
| 162 | 137 | 140 | 4.6 | 4.2 | 100 | 104 | 7.6 | 4.0 | 0.060 | 0.072 | 2.52 | 2.41 | 1.35 | 1.28 |

* Out of normal range. Not clinically significant

Table 12.1.8.3: Biochemistry Values (cont.) per Subject

| Patient No. | Bilirubin (0 - 17 umol/L) | | Alk Phosphate (30 - 115 U/L) | | ALT (5 - 40 U/L) | | AST (5 - 40 U/L) | | GGT (≤ 66 U/L) | | Magnesium (0.7 - 1.0 mmol/L) | | Glucose (3.3 - 7.8 mmol/L) | |
|-------------|------------------------------|---------|---------------------------------|---------|---------------------|---------|---------------------|---------|-------------------------|---------|---------------------------------|---------|-------------------------------|---------|
| | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 101 | 8 | 9 | 61 | 63 | 27 | 25 | 17 | 19 | 31 | 28 | 0.9 | 1.0 | 5.9* | 5.3 |
| 102 | 11 | 13 | 58 | 56 | 22 | 24 | 19 | 21 | 23 | 20 | 0.9 | N/A | 5.6 | 4.4 |
| 103 | 15 | 23 | 72 | 63 | 21 | 28 | 18 | 37 | 13 | 10 | 0.8 | 0.9 | 6.4 | 4.6 |
| 104 | 12 | 22 | 66 | 71 | 25 | 35 | 19 | 29 | 35 | 31 | 1.0 | 1.1* | 4.5 | 4.7 |
| 105 | 15 | 9 | 45 | 50 | 10 | 13 | 18 | 19 | 9 | 12 | 1.1* | 0.8 | 4.0 | 4.3 |
| 106 | 5 | 10 | 81 | 84 | 11 | 14 | 19 | 23 | 16 | 12 | 0.94 | 0.92 | 4.4 | 4.1 |
| 107 | 8 | 13 | 92 | 97 | 10 | 10 | 19 | 19 | 10 | 11 | 0.9 | 1.1* | 4.6 | 4.7 |
| 108 | 17 | 12 | 76 | 69 | 20 | 19 | 21 | 23 | 25 | 17 | 1.0 | 0.9 | 4.8 | 4.5 |
| 109 | 9 | 23* | 91 | 71 | 16 | 18 | 19 | 23 | 18 | 16 | 0.8 | 0.9 | 4.6 | 4.6 |
| 110 | 13 | 21* | 81 | 68 | 54* | 36 | 31 | 32 | 33 | 27 | 0.9 | 1.0 | 9.1* | 4.1 |
| 111 | 12 | 16 | 62 | 63 | 78* | 93* | 32 | 40 | 25 | 24 | 0.9 | 1.1* | 5.0 | 4.7 |
| 112 | 5 | 9 | 62 | 60 | 12 | 15 | 16 | 21 | 16 | 15 | 0.9 | 1.0 | 4.6 | 4.0 |
| 113 | 16 | 45* | 55 | 49 | 33 | 31 | 24 | 25 | 19 | 17 | 0.9 | 1.0 | 5.1 | 3.4 |
| 114 | 17 | 15 | 78 | 71 | 33 | 27 | 34 | 27 | 20 | 18 | 1.0 | 1.0 | 3.5 | 4.4 |
| 115 | 13 | 16 | 48 | 49 | 47* | 47* | 38 | 37 | 17 | 19 | 1.0 | 1.0 | 4.8 | 4.2 |
| 116 | 12 | 18* | 72 | 65 | 25 | 22 | 27 | 27 | 13 | 14 | 0.8 | 1.1* | 4.4 | 4.6 |
| 117 | 10 | 17 | 43 | 35 | 18 | 18 | 17 | 19 | 12 | 13 | 0.9 | 1.1* | 4.6 | 3.8 |
| 118 | 9 | 14 | 73 | 71 | 24 | 18 | 28 | 26 | 14 | 13 | 0.9 | 0.9 | 4.8 | 4.1 |
| 119 | 8 | 20* | 66 | 70 | 18 | 15 | 19 | 18 | 21 | 19 | 0.8 | N/A | 4.3 | 4.2 |
| 120 | 5 | 9 | 63 | 67 | 18 | 20 | 19 | 22 | 10 | 10 | 0.7 | 0.9 | 3.3 | 4.3 |
| 121 | 5 | N/A | 81 | N/A | 43 | N/A | 25 | N/A | 62 | N/A | 0.9 | N/A | 3.7 | N/A |
| 122 | 7 | 43 | 45 | 52 | 21 | 23 | 19 | 26 | 23 | 21 | 0.9 | 1.0 | 4.8 | 4.5 |
| 123 | 3 | 7 | 75 | 65 | 26 | 25 | 18 | 21 | 29 | 23 | 0.8 | 0.8 | 4.3 | 3.0 |
| 124 | 11 | 17 | 66 | 64 | 13 | 7 | 20 | 22 | 9 | 8 | N/A | 1.0 | 4.1 | 4.1 |
| 125 | 8 | 17 | 80 | 84 | 48* | 55* | 29 | 32 | 23 | 23 | 0.9 | 1.0 | 4.3 | 4.7 |

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|-----|----|-----|-----|------|-----|----|----|----|------|------|-----|-----|-----|-----|
| 126 | 5 | 10 | 65 | 68 | 26 | 25 | 19 | 18 | 32 | 28 | N/A | 1.0 | 5.6 | 4.1 |
| 127 | 14 | 36* | 58 | 58 | 15 | 11 | 19 | 21 | 8 | 9 | 0.9 | 0.9 | 5.1 | 4.0 |
| 128 | 12 | 16 | 82 | 80 | 15 | 13 | 23 | 23 | 13 | 16 | 0.9 | 1.0 | 5.1 | 4.4 |
| 129 | 6 | 11 | 52 | 52 | 45* | 34 | 23 | 25 | 41 | 32 | 1.0 | 1.0 | 5.1 | 5.0 |
| 130 | 10 | 9 | 63 | 56 | 8 | 8 | 14 | 13 | 13 | 10 | 0.9 | 1.0 | 4.2 | 4.6 |
| 131 | 13 | 20* | 63 | 66 | 27 | 30 | 22 | 30 | 23 | 22 | 0.8 | 1.0 | 4.9 | 4.4 |
| 132 | 6 | 11 | 67 | 51 | 24 | 25 | 27 | 33 | 20 | 17 | 0.8 | 1.0 | 5.0 | 4.8 |
| 133 | 6 | 12 | 55 | 66 | 22 | 18 | 25 | 21 | 18 | 16 | 0.8 | 0.9 | 4.8 | 3.8 |
| 134 | 8 | 15 | 41 | 30 | 23 | 28 | 24 | 28 | 46 | 47 | 0.8 | 0.9 | 6.1 | 5.3 |
| 135 | 13 | 23* | 114 | 117* | 36 | 30 | 33 | 31 | 442* | 424* | 0.8 | 0.9 | 4.6 | 4.1 |
| 136 | 9 | 16 | 93 | 923 | 17 | 18 | 22 | 25 | 18 | 16 | 0.8 | 0.8 | 3.4 | 4.5 |

* Out of normal range. Not clinically significant

Table 12.1.8.4: Serum Osmolality Values per Subject per Arm

| Glycoplep | | | Hypertonic | | PicoPrep Sachets | | PicoPrep Capsules | |
|-----------|--------|--------|------------|--------|------------------|--------|-------------------|---------------|
| Pt No. | V1 | V2 | Pt No. | V1 | V2 | Pt No. | V1 | V2 |
| 103 | 284 | 286 | 107 | 287 | 290 | 104 | 295 | 285 |
| 106 | 285 | 285 | 114 | 289 | 286 | 105 | 288 | 284 |
| 108 | 288 | 288 | 116 | 279 | 286 | 109 | 285 | 282 |
| 113 | 298 | 294 | 117 | 286 | 285 | 112 | 299 | 292 |
| 115 | 295 | 292 | 118 | 291 | 288 | 130 | 285 | 288 |
| 119 | 301 | 284 | 120 | 286 | 280 | 133 | 299 | 316 |
| 121 | N/A | N/A | 122 | 297 | 293 | 140 | 298 | 299 |
| 123 | 283 | 282 | 131 | 294 | 298 | 141 | 289 | 283 |
| 127 | 289 | 289 | 132 | 300 | 288 | 142 | 298 | 302 |
| 136 | 301 | 297 | 134 | 287 | 278 | 143 | 281 | 286 |
| 146 | 293 | 280 | 137 | 297 | 287 | 145 | 280 | 256 |
| 148 | 288 | 292 | 147 | 298 | 292 | 149 | 284 | Not Available |
| 151 | 296 | 291 | 153 | 288 | 295 | 152 | 295 | |
| 157 | 284 | 302 | 155 | 296 | 288 | 154 | 293 | |
| 160 | N/A | N/A | 159 | 309 | 288 | | | |
| 161 | 304 | 288 | | | | | | |
| Mean | 292.07 | 289.29 | | 292.27 | 288.13 | | 290.64 | 289.31 |
| St Dev | 7.16 | 5.95 | | 7.44 | 5.18 | | 6.88 | 13.94 |
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Table 12.1.8.5: Urinalysis Values per Subject

| Patient Number | Sodium (35-180 mmol/L) | | Potassium (25-75 mmol/L) | | Chloride (122-135 mmol/L) | | Osmolarity (100-800 mmol/Kg) | | Specific Gravity (1.005 – 1.030) | |
|----------------|---------------------------|---------|-----------------------------|---------|------------------------------|---------|---------------------------------|---------|-------------------------------------|---------|
| | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 101 | 110 | 62 | 31 | 120* | 112* | N/A | 693 | 693 | 1.019 | 1.012 |
| 102 | N/A | N/A | N/A | N/A | N/A | N/A | 899* | 742 | 1.024 | 1.023 |
| 103 | N/A | N/A | N/A | N/A | N/A | N/A | 525 | 663 | 1.013 | 1.021 |
| 104 | N/A | 4* | N/A | 2* | N/A | N/A | 50* | 695 | 1.001* | N/A |
| 105 | 28* | 82 | 44 | 11 | 24* | 103 | 368 | 680 | 1.012 | 1.021 |
| 106 | 15* | 37 | 17* | 12* | 21* | 30* | 97* | 189 | 1.003* | 1.006 |
| 107 | 66 | 140 | 46 | 16* | 80* | 136* | 432 | 503 | 1.011 | 1.013 |
| 108 | 91 | 120 | 116* | 27 | 114* | 94* | 718 | 369 | 1.020 | 1.010 |
| 109 | 66 | 40 | 113* | 3 | 83* | 40* | 799 | 210 | 1.025 | 1.006 |
| 110 | 117 | 146 | 136* | 53 | 152* | 119* | 878* | 583 | 1.024 | 1.015 |
| 111 | 127 | 145 | 86* | 90* | 145* | 165* | 669 | 610 | 1.017 | 1.015 |
| 112 | 99 | 51 | 82* | 29 | 114* | 51* | 820* | 359 | 1.026 | 1.010 |
| 113 | 136 | 159 | 66 | 53 | 147* | N/A | 698 | 1034* | 1.026 | 1.029 |
| 114 | 82 | 58 | 93* | 62 | 132 | 91* | 567 | 377 | 1.014 | 1.010 |
| 115 | 80 | 66 | 93* | 184* | 113* | 78* | 1052* | 1094* | 1.031* | 1.034* |
| 116 | 36 | 22 | 26 | 35 | 50* | N/A | 281 | 324 | 1.007 | 1.010 |
| 117 | 66 | 41 | 24* | 16* | 65* | 50* | 342 | 221 | 1.010 | 1.007 |
| 118 | 125 | 39 | 81* | 45 | 153* | 42* | 675 | 600 | 1.017 | 1.019 |
| 119 | 146 | 115 | 114* | 51 | 216* | 105* | 947* | 499 | 1.024 | 1.013 |
| 120 | 130 | 96 | 76* | 54 | 181* | 125 | 811* | 627 | 1.023 | 1.018 |
| 121 | 179 | N/A | 89* | N/A | 173* | N/A | 1058* | N/A | 1.029 | N/A |
| 122 | 107 | 18* | 76* | 18* | 139* | 20* | 572 | 155 | 1.014 | 1.004* |
| 123 | 174 | 228* | 52 | 23 | 201* | 83* | 954* | 912* | 1.027 | 1.025 |
| 124 | 179 | 124 | 89* | 32 | 173* | 54* | 1058* | 659 | 1.029 | 1.020 |
| 125 | 141 | 80 | 62 | 21* | 138* | 51* | 754 | 434 | 1.019 | 1.013 |
| 126 | 115 | 82 | 65 | 64 | 130 | 94 | 662 | 681 | 1.017 | 1.019 |
| 127 | 94 | 40 | 90* | 13* | 121* | 19* | 598 | 159 | 1.016 | 1.004* |
| 128 | 110 | 75 | 122* | 117* | 149* | 58* | 816* | 477 | 1.022 | 1.013 |
| 129 | 61 | 143 | 78* | 21* | N/A | N/A | 485 | 619 | 1.012 | 1.017 |
| 130 | 91 | 95 | 41 | 39 | 127 | N/A | 853* | 1062* | 1.023 | 1.030 |
| 131 | 43 | 124 | 98* | 39 | 82* | 110* | 839* | 492 | 1.024 | 1.012 |
| 132 | 83 | 101 | 39 | 39 | 91* | 88* | 514 | 375 | 1.013 | 1.010 |
| 133 | 41 | 90 | 11* | 13* | 35* | 59* | 161 | 540 | 1.003* | 1.016 |

| | Sodium (35-180 mmol/L) | | Potassium (25-75 mmol/L) | | Chloride (122-135 mmol/L) | | Osmolarity (100-800 mmol/Kg) | | Specific Gravity (1.005 – 1.030) | |
|----------------|---------------------------|---------|-----------------------------|---------|------------------------------|---------|---------------------------------|---------|-------------------------------------|---------|
| Patient Number | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 | Baseline | Visit 2 |
| 134 | 112 | 43 | 97* | 108* | 175* | 46* | 963* | 675 | 1.027 | 1.024 |
| 135 | 53 | 64 | 44 | 24* | 66* | 35* | 630 | 617 | 1.019 | 1.019 |
| 136 | 50 | 201* | 35 | 52 | 55* | 88* | 474 | 709 | 1.013 | 1.021 |
| 137 | 94 | 52 | 84* | 48 | 121* | 46 | 993* | 357 | 1.024 | 1.010 |
| 138 | 51 | N/A | 111* | N/A | 73* | N/A | 656 | N/A | 1.019 | N/A |
| 139 | 141 | 228 | 239* | 17 | 280* | N/A | 1091* | 262 | N/A | 1.020 |
| 140 | 46 | 89 | 103* | 40 | 57* | 76* | 931* | 415 | 1.027 | 1.011 |
| 141 | 42 | 18 | 86* | 7* | 73* | 20* | 645 | 179 | 1.019 | 1.005 |
| 142 | 72 | 134 | 217* | 33 | 133 | 99* | 785 | 501 | 1.023 | 1.014 |
| 143 | 63 | 133 | 30 | 89* | 72* | 113* | 315 | 616 | 1.009 | 1.015 |
| 144 | 41 | 18 | 47 | 2* | 63* | 8* | 337 | 72* | 1.008 | 1.002* |
| 145 | 9* | 42 | 36 | 72 | 23* | 19* | 156 | 550 | 1.005 | 1.017 |
| 146 | 161 | 207 | 140* | 214 | 152* | 123 | 947* | 924 | 1.027 | 1.027 |
| 147 | 158 | 37 | 130* | 28 | 221* | 46* | 1012* | 216 | 1.026 | 1.006 |
| 148 | 96 | 158 | 24* | 51 | 96* | 118* | 337 | 603 | 1.008 | 1.016 |
| 149 | 166 | 67 | 87* | 21 | 230* | 29 | 681 | N/A | 1.016 | N/A |
| 150 | 138 | 65 | 50 | 15* | 211* | 55* | 781 | 341 | 1.019 | 1.009 |
| 151 | 169 | 131 | 110* | 42 | 193* | 38* | 1061* | 662 | 1.027 | 1.020 |
| 152 | 92 | 23* | 93* | 10* | 101* | 27* | 662 | 244 | 1.018 | 1.007 |
| 153 | 106 | 22* | 54 | 4* | 137* | 16* | 654 | 110 | 1.020 | 1.003* |
| 154 | 38 | 74 | 45 | 19 | 39* | 83* | 348 | 349 | 1.010 | 1.010 |
| 155 | 46 | 85 | 69 | 38 | 104* | 76* | 584 | 682 | 1.017 | 1.021 |
| 156 | 118 | 35 | 85* | 22* | 162* | N/A | 876* | 537 | 1.023 | 1.015 |
| 157 | 41* | 96 | 10* | 43 | 41* | N/A | 170 | 658 | 1.004* | 1.021 |
| 158 | 131 | 175 | 111* | 13* | 165* | 120* | 922* | 875* | 1.024 | 1.023 |
| 159 | 137 | 156 | 44 | 86 | 110* | 132 | 586 | 927* | 1.016 | 1.026 |
| 160 | 156 | N/A | 86* | N/A | 132 | N/A | 927* | N/A | 1.026 | N/A |
| 161 | 49 | 86 | 30 | 27 | 57* | 57* | 397 | 315 | 1.011 | 1.008 |
| 162 | 59 | 101 | 33 | 21* | 65* | 109* | 306 | 424 | 1.007 | 1.012 |

12.1.9 Relevant Medical History of eligible subjects

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Arm | Completion Status | Relevant Medical History |
|----------------|----------|---------------|----------|----------|--|-------------------|-------------------------------|
| 101 | G-R | 09/08/47 | 17/07/03 | Yes | PicoPrep™ Capsules | Completed | IBS, polyps |
| 102 | R-R | 18/01/52 | 17/07/03 | Yes | PicoPrep™ Capsules | Completed | Haemorrhoids |
| 103 | YSA | 26/07/50 | 17/07/03 | Yes | Standard Glycoprep™ | Completed | Constipation |
| 104 | T-D | 08/08/46 | 22/07/03 | Yes | Standard PicoPrep™ | Completed | Haemorrhoids, GORD |
| 105 | KCF | 26/04/75 | 24/07/03 | Yes | Standard PicoPrep™ | Completed | Crohn's disease |
| 106 | S-V | 19/03/64 | 06/08/03 | Yes | Standard Glycoprep™ | Completed | Nil |
| 107 | T-C | 25/01/44 | 06/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 108 | F-L | 23/05/42 | 07/08/03 | Yes | Standard Glycoprep™ | Completed | Nil |
| 109 | M-T | 30/04/44 | 07/08/03 | Yes | Standard PicoPrep™ | Completed | Diverticular disease, polyps |
| 110 | R-G | 23/08/53 | 12/08/03 | Yes | PicoPrep™ Capsules | Completed | Gastritis |
| 111 | BRH | 03/09/63 | 14/08/03 | Yes | PicoPrep™ Capsules | Completed | Acute diverticulitis, colitis |
| 112 | G-C | 02/03/63 | 14/08/03 | Yes | Standard PicoPrep™ | Completed | Colonic polyps |
| 113 | R-S | 26/09/71 | 14/08/03 | Yes | Standard Glycoprep™ | Completed | D-IBS |
| 114 | KGT | 28/05/76 | 15/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | GORD |
| 115 | N-L | 22/05/45 | 18/08/03 | Yes | Standard Glycoprep™ | Completed | Constipation |
| 116 | A-P | 07/07/77 | 18/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Polyps |
| 117 | B-D | 31/10/56 | 18/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Diarrhoea |
| 118 | JEP | 12/02/38 | 11/09/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Diarrhoea |
| 119 | R-W | 11/01/61 | 11/09/03 | Yes | Standard Glycoprep™ | Completed | Polyps |
| 120 | BAW | 31/01/60 | 12/09/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Polyps |

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Arm | Completion Status | Relevant Medical History |
|----------------|----------|---------------|----------|----------|--|-------------------|-----------------------------------|
| 121 | MAM | 30/04/70 | 12/09/03 | Yes | Standard Glycoprep™ | Delayed Exclusion | Constipation |
| 122 | SGD | 22/01/56 | 17/09/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Haemorrhoids |
| 123 | DKH | 28/07/76 | 17/09/03 | Yes | Standard Glycoprep™ | Completed | Diarrhoea |
| 124 | M-A | 05/01/59 | 17/09/03 | Yes | PicoPrep™ Capsules | Completed | Diarrhoea |
| 125 | G-W | 04/10/45 | 17/09/03 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 126 | AMM | 19/12/62 | 17/09/03 | Yes | PicoPrep™ Capsules | Completed | Constipation |
| 127 | SJE | 27/04/54 | 19/09/03 | Yes | Standard Glycoprep™ | Completed | Haemorrhoids |
| 128 | ADW | 03/10/56 | 13/10/03 | Yes | PicoPrep™ Capsules | Completed | Constipation dominant IBS |
| 129 | P-H | 10/06/58 | 16/10/03 | Yes | PicoPrep™ Capsules | Completed | Polyps |
| 130 | J-S | 31/07/81 | 31/10/03 | Yes | Standard PicoPrep™ | Completed | Crohn's disease |
| 131 | F-T | 01/01/63 | 06/11/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Polyps/adenoma |
| 132 | KHL | 24/12/44 | 07/11/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Sigmoid carcinoma |
| 133 | JCE | 28/03/57 | 19/01/04 | Yes | Standard PicoPrep™ | Completed | Anal fissure |
| 134 | M-M | 20/09/38 | 19/01/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Diverticular disease, polyps |
| 135 | PEB | 30/04/56 | 20/01/04 | Yes | PicoPrep™ Capsules | Completed | Ulcerative colitis, pseudo-polyps |
| 136 | FAW | 25/07/54 | 06/02/04 | Yes | Standard Glycoprep™ | Completed | Haemorrhoids |
| 137 | RSM | 29/01/72 | 06/02/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 138 | GMC | 25/07/44 | 06/02/04 | Yes | PicoPrep™ Capsules | Withdrawn | Polyps |
| 139 | AEN | 22/04/42 | 09/02/04 | Yes | PicoPrep™ Capsules | Completed | Haemorrhoids, polyps |
| 140 | RCW | 02/01/52 | 12/02/04 | Yes | Standard PicoPrep™ | Completed | Colonic polyps |
| 141 | C-W | 14/04/60 | 12/02/04 | Yes | Standard PicoPrep™ | Completed | IBS |
| 142 | G-F | 30/03/43 | 12/02/04 | Yes | Standard PicoPrep™ | Completed | Nil |

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Arm | Completion Status | Relevant Medical History |
|----------------|----------|---------------|----------|----------|--|-------------------|---|
| 143 | MFB | 14/09/70 | 19/02/04 | Yes | Standard PicoPrep™ | Completed | IBS, haemorrhoids |
| 144 | M-V | 21/08/67 | 19/02/04 | Yes | PicoPrep™ Capsules | Completed | Polyps |
| 145 | B-W | 06/03/52 | 19/02/04 | Yes | Standard PicoPrep™ | Completed | Haemorrhoids |
| 146 | JAK | 28/03/84 | 20/02/04 | Yes | Standard Glycoprep™ | Completed | Fissure |
| 147 | P-F | 02/04/67 | 20/02/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Polyps |
| 148 | SJW | 23/04/71 | 05/03/04 | Yes | Standard Glycoprep™ | Completed | IBS, diarrhoea |
| 149 | D-C | 26/05/67 | 11/03/04 | Yes | Standard PicoPrep™ | Completed | Ulcerative colitis, diarrhoea |
| 150 | G-C | 05/11/47 | 11/03/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 151 | S-A | 06/12/72 | 12/03/04 | Yes | Standard Glycoprep™ | Completed | Nil |
| 152 | PGB | 10/03/52 | 15/03/04 | Yes | Standard PicoPrep™ | Completed | Polyps |
| 153 | AMG | 05/11/35 | 19/03/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Diarrhoea |
| 154 | P-Q | 13/06/49 | 19/03/04 | Yes | Standard PicoPrep™ | Completed | Haemorrhoids |
| 155 | M-R | 04/12/62 | 26/03/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 156 | RST | 14/03/50 | 29/03/04 | Yes | PicoPrep™ Capsules | Completed | GORD |
| 157 | C-A | 16/12/74 | 31/03/04 | Yes | Standard Glycoprep™ | Completed | Nil |
| 158 | EWP | 08/10/52 | 07/04/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 159 | D-B | 10/04/46 | 08/04/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 160 | A-G | 01/02/61 | 14/04/04 | Yes | Standard Glycoprep™ | Withdrawn | n/a |
| 161 | GRN | 21/08/49 | 19/04/04 | Yes | Standard Glycoprep™ | Completed | Nil |
| 162 | M-A | 11/05/59 | 30/04/04 | Yes | PicoPrep™ Capsules | Completed | Crohn's disease, haemorrhoids, anal fissure |

12.2.10: Baseline Complaints as reported separately to Medical History

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Arm | Completion Status | Baseline symptoms |
|----------------|----------|---------------|----------|----------|--|-------------------|-------------------------------|
| 101 | G-R | 09/08/47 | 17/07/03 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 102 | R-R | 18/01/52 | 17/07/03 | Yes | PicoPrep™ Capsules | Completed | Perianal burning, PR bleeding |
| 103 | YSA | 26/07/50 | 17/07/03 | Yes | Standard Glycoprep™ | Completed | Cramps, bloating |
| 104 | T-D | 08/08/46 | 22/07/03 | Yes | Standard PicoPrep™ | Completed | PR bleeding |
| 105 | KCF | 26/04/75 | 24/07/03 | Yes | Standard PicoPrep™ | Completed | Diarrhoea, rectal bleeding |
| 106 | S-V | 19/03/64 | 06/08/03 | Yes | Standard Glycoprep™ | Completed | PR bleeding |
| 107 | T-C | 25/01/44 | 06/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 108 | F-L | 23/05/42 | 07/08/03 | Yes | Standard Glycoprep™ | Completed | Flatulence |
| 109 | M-T | 30/04/44 | 07/08/03 | Yes | Standard PicoPrep™ | Completed | Nil |
| 110 | R-G | 23/08/53 | 12/08/03 | Yes | PicoPrep™ Capsules | Completed | Abdominal pain |
| 111 | BRH | 03/09/63 | 14/08/03 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 112 | G-C | 02/03/63 | 14/08/03 | Yes | Standard PicoPrep™ | Completed | Ongoing fissure |
| 113 | R-S | 26/09/71 | 14/08/03 | Yes | Standard Glycoprep™ | Completed | Nil |
| 114 | KGT | 28/05/76 | 15/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Diarrhoea |
| 115 | N-L | 22/05/45 | 18/08/03 | Yes | Standard Glycoprep™ | Completed | PR bleeding |
| 116 | A-P | 07/07/77 | 18/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Constipated |
| 117 | B-D | 31/10/56 | 18/08/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Bloating, burping |
| 118 | JEP | 12/02/38 | 11/09/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Diarrhoea |
| 119 | R-W | 11/01/61 | 11/09/03 | Yes | Standard Glycoprep™ | Completed | Nil |
| 120 | BAW | 31/01/60 | 12/09/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | PR bleeding |

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Arm | Completion Status | Baseline Symptoms |
|----------------|----------|---------------|----------|----------|--|-------------------|---------------------------------|
| 121 | MAM | 30/04/70 | 12/09/03 | Yes | Standard Glycoprep™ | Delayed Exclusion | Constipated |
| 122 | SGD | 22/01/56 | 17/09/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | PR bleeding |
| 123 | DKH | 28/07/76 | 17/09/03 | Yes | Standard Glycoprep™ | Completed | Abdominal pain, diarrhoea |
| 124 | M-A | 05/01/59 | 17/09/03 | Yes | PicoPrep™ Capsules | Completed | Abdominal pain |
| 125 | G-W | 04/10/45 | 17/09/03 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 126 | AMM | 19/12/62 | 17/09/03 | Yes | PicoPrep™ Capsules | Completed | PR bleeding |
| 127 | SJE | 27/04/54 | 19/09/03 | Yes | Standard Glycoprep™ | Completed | PR bleeding |
| 128 | ADW | 03/10/56 | 13/10/03 | Yes | PicoPrep™ Capsules | Completed | PR bleeding |
| 129 | P-H | 10/06/58 | 16/10/03 | Yes | PicoPrep™ Capsules | Completed | Indigestion |
| 130 | J-S | 31/07/81 | 31/10/03 | Yes | Standard PicoPrep™ | Completed | Nil |
| 131 | F-T | 01/01/63 | 06/11/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 132 | KHL | 24/12/44 | 07/11/03 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 133 | JCE | 28/03/57 | 19/01/04 | Yes | Standard PicoPrep™ | Completed | PR bleeding |
| 134 | M-M | 20/09/38 | 19/01/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 135 | PEB | 30/04/56 | 20/01/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 136 | FAW | 25/07/54 | 06/02/04 | Yes | Standard Glycoprep™ | Completed | PR bleeding |
| 137 | RSM | 29/01/72 | 06/02/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 138 | GMC | 25/07/44 | 06/02/04 | Yes | PicoPrep™ Capsules | Withdrawn | Nil |
| 139 | AEN | 22/04/42 | 09/02/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 140 | RCW | 02/01/52 | 12/02/04 | Yes | Standard PicoPrep™ | Completed | Nil |
| 141 | C-W | 14/04/60 | 12/02/04 | Yes | Standard PicoPrep™ | Completed | Bleeding, constipated, bloating |
| 142 | G-F | 30/03/43 | 12/02/04 | Yes | Standard PicoPrep™ | Completed | Nil |

| Patient Number | Initials | Date Of Birth | Consent | Enrolled | Arm | Completion Status | Baseline Symptoms |
|----------------|----------|---------------|----------|----------|--|-------------------|----------------------------|
| 143 | MFB | 14/09/70 | 19/02/04 | Yes | Standard PicoPrep™ | Completed | Bleeding |
| 144 | M-V | 21/08/67 | 19/02/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 145 | B-W | 06/03/52 | 19/02/04 | Yes | Standard PicoPrep™ | Completed | Nil |
| 146 | JAK | 28/03/84 | 20/02/04 | Yes | Standard Glycoprep™ | Completed | Nil |
| 147 | P-F | 02/04/67 | 20/02/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 148 | SJW | 23/04/71 | 05/03/04 | Yes | Standard Glycoprep™ | Completed | Diarrhoea, cramping |
| 149 | D-C | 26/05/67 | 11/03/04 | Yes | Standard PicoPrep™ | Completed | PR bleeding, diarrhoea |
| 150 | G-C | 05/11/47 | 11/03/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 151 | S-A | 06/12/72 | 12/03/04 | Yes | Standard Glycoprep™ | Completed | Abdominal pain, flatulence |
| 152 | PGB | 10/03/52 | 15/03/04 | Yes | Standard PicoPrep™ | Completed | Nil |
| 153 | AMG | 05/11/35 | 19/03/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | PR bleeding, diarrhoea |
| 154 | P-Q | 13/06/49 | 19/03/04 | Yes | Standard PicoPrep™ | Completed | Nil |
| 155 | M-R | 04/12/62 | 26/03/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 156 | RST | 14/03/50 | 29/03/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 157 | C-A | 16/12/74 | 31/03/04 | Yes | Standard Glycoprep™ | Completed | Nil |
| 158 | EWP | 08/10/52 | 07/04/04 | Yes | PicoPrep™ Capsules | Completed | Nil |
| 159 | D-B | 10/04/46 | 08/04/04 | Yes | Hypertonic Solution and PicoPrep™ Capsules | Completed | Nil |
| 160 | A-G | 01/02/61 | 14/04/04 | Yes | Standard Glycoprep™ | Withdrawn | Nil |
| 161 | GRN | 21/08/49 | 19/04/04 | Yes | Standard Glycoprep™ | Completed | Nil |
| 162 | M-A | 11/05/59 | 30/04/04 | Yes | PicoPrep™ Capsules | Completed | Constipation |

12.2 Study Information

12.2.1 HREC Involved in the Approval of the Study

Centre for Digestive Diseases Human Research Ethics Committee
144 Great North Road
Five Dock, NSW, 2046

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Fax: +61 2 9713 1026

12.2.2 List of Investigators and Other Study Staff (CV's included on following pages)

| | | |
|-------------------------------|---------------------|---------|
| Principle Investigator | Dr Thomas Borody | Page 69 |
| Co-Investigator 1 | Dr Antony Wettstein | Page 70 |
| Co-Investigator 2 | Dr Sanjay Ramrahka | Page 71 |
| Co-Investigator 3 | Dr John Saxon | Page 72 |

CV - Thomas Borody

| | |
|----------------------|-----------------------------|
| Thomas Julius Borody | MD, MBBS, FRACP, FACG, FACP |
|----------------------|-----------------------------|

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Education and Training (List all Colleges, Universities and Medical Schools attended through postdoctoral/fellowship training, including board certification/medical license)

| Name and Location of Institution (State or Province and Country) | Degree and Year Awarded |
|---|---|
| American College of Physicians (Philadelphia, USA) | FACP 2002 |
| American College of Physicians (Philadelphia, USA) | FACG 1993 |
| University of NSW (NSW, Australia) | MD 1984 |
| Royal Australasian College of Physicians (NSW, Australia) | FRACP 1982 |
| University of New South Wales (NSW, Australia) | MBBS 1974 |
| New South Wales Medical Board (NSW, Australia) | Current New South Wales Registration, Australia Registration Number: MPO: 013614 First Registered 1975 |
| University of New South Wales (NSW, Australia) | BSc (Med) Hons 1971 |

Professional Experience

| Position/Title | Name and Location of Institution (State or Province and Country) | Dates |
|---------------------------------|---|-----------------|
| Director and Gastroenterologist | Centre for Digestive Diseases (NSW, Australia) | 1985 to Current |
| Consulting Gastroenterologist | Sydney Adventist Hospital (NSW, Australia) | 1995 to Current |

CV – Antony Wettstein

| | |
|-------------------------|-------------------|
| Antony Robert Wettstein | MBBS(Hons), FRACP |
|-------------------------|-------------------|

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Education and Training (List all Colleges, Universities and Medical Schools attended through postdoctoral/fellowship training, including board certification/medical license)

| Name and Location of Institution (State or Province and Country) | Degree and Year Awarded |
|--|---|
| Royal Australasian College of Physicians (NSW, Australia) | FRACP 1995 |
| University of New South Wales (NSW, Australia) | MBBS 1990 |
| University of New South Wales (NSW, Australia) | Bachelor of Surgery |
| New South Wales Medical Board (NSW, Australia) | Current New South Wales Registration, Australia Registration Number: MPO: 276951 First Registered 1991 |

Professional Experience

| Position/Title | Name and Location of Institution (State or Province and Country) | Dates |
|---------------------------------|--|-----------------|
| Consulting Gastroenterologist | Centre for Digestive Diseases (NSW, Australia) | 2000 to Current |
| Consulting Gastroenterologist | Diagnostic Endoscopy Centre St Vincent's Clinic, (NSW, Australia) | 2000 to Current |
| Locum VMO Gastroenterologist | St Vincent's Public Hospital (NSW, Australia) | 2002 to Current |

CV – Sanjay Ramrakha

| | |
|-----------------------|---------------------|
| Sanjay Chand Ramrakha | MBBS, FRACGP, FACEM |
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Education and Training (List all Colleges, Universities and Medical Schools attended through postdoctoral/fellowship training, including board certification/medical license)

| Name and Location of Institution (State or Province and Country) | Degree and Year Awarded |
|--|---|
| Australian College of Emergency Medicine (NSW, Australia) | FACEM 1999 |
| Royal Australasian College of Physicians (NSW, Australia) | FRACGP 1998 |
| University of New South Wales (NSW, Australia) | MBBS 1987 |
| New South Wales Medical Board (NSW, Australia) | Current New South Wales Registration, Australia Registration Number: MPO: 226951 First Registered 1988 |

Professional Experience

| Position/Title | Name and Location of Institution (State or Province and Country) | Dates |
|--------------------------------------|--|-----------------|
| Sedationist | Centre for Digestive Diseases (NSW, Australia) | 1999 to Current |
| Staff Specialist – Emergency Dept | Royal Prince Alfred Hospital (NSW, Australia) | 1999 to Current |
| Staff Specialist – Emergency Dept | Liverpool Hospital (NSW, Australia) | 2005 to Current |

CV – John Saxon

| | |
|--------------------|--------------------|
| John Anthony Saxon | MBBS, FRACP, FACEM |
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Education and Training (List all Colleges, Universities and Medical Schools attended through postdoctoral/fellowship training, including board certification/medical license)

| Name and Location of Institution (State or Province and Country) | Degree and Year Awarded |
|--|---|
| Australian College of Emergency Medicine (NSW, Australia) | 1998 |
| Royal Australasian College of Physicians (NSW, Australia) | FRACP 1987 |
| University of New South Wales (NSW, Australia) | MBBS 1984 |
| New South Wales Medical Board (NSW, Australia) | Current New South Wales Registration, Australia Registration Number: MPO: 208195 First Registered 1985 |

Professional Experience

| Position/Title | Name and Location of Institution (State or Province and Country) | Dates |
|-----------------------|--|-----------------|
| Sedationist | Centre for Digestive Diseases (NSW, Australia) | 1995 to Current |
| Sedationist | Rosemount Endoscopy Centre (NSW, Australia) | 2000 to Current |
| Chief Medical Officer | Sydney Turf Club and Australian Jockey Club (NSW, Australia) | 1999 to Current |

Calculation of amount of sodium salt and sugar in the compositions of Kawakami

a. Sodium salt

The composition described in Kawakami is a 900 mL solution that includes 4.8-5.4 mM sodium chloride, 8.5-9.3 mM potassium hydrate and 10.7-2.1 grams sugar. Sodium chloride has a molecular weight of 58.45 (The Merck Index, 9th ed. (1976), entry **8343**, page 1111). Thus, the amount of sodium chloride in the composition described in Kawakami ranges from about 0.25-0.29 grams, as shown below.

$$58.45 \text{ g/L} = 1 \text{ M} \therefore 0.05845 \text{ g/L} = 1 \text{ mM}$$

The composition contains 900 mL of 4.8-5.4 mM NaCl. Therefore, the composition contains:

$$4.8 \times 0.05845 \text{ g/L} = 0.28 \text{ g/L}; 900 \text{ mL of this solution contains } 0.25 \text{ g NaCl.}$$

$$5.4 \times 0.05845 \text{ g/L} = 0.32 \text{ g/L}; 900 \text{ mL of this solution contains } 0.29 \text{ g NaCl.}$$

b. Sugar

The composition of Kawakami contains 2.1 to 10.7 grams of sugar. Hence, the ratio of sugar to sodium salt in the compositions described in Kawakami range from about 7.3 times the weight of the sodium salt (2.1 g sugar/0.29 g NaCl) to about 42.8 times the weight of the sodium salt (10.7 g sugar/0.25 g NaCl).

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Printed in the U. S. A.

as antiseptic, detergent,

Compound. Dobell's ate, 1.5 g sodium bicar- ml glycerol and water to

embranes.
is a nonirritant wash for

sodium tetrahydroborate. H 10.65%, Na 60.77%. ate and sodium hydride. *J. Am. Chem. Soc.* 75, other metal tetrahydro- *org. Chem* 11, 99-231

ng a dihydrate, mp 36-) is stable in dry air to at 500°. Supports com- 55%; at 60°: 88.5%; liq mine at 75°: 22%; mor- 3.1%; methanol at 20°: (reacts slowly); tetrahy- (reacts slowly); tetrahy- 5°: 5.5%; dimethylform- most stable in the pres- % for a nearly satd soln for several days. Solns

des, ketones and Schiff o reduces acids, esters, organic anions. Further ing agent, as scavenger d peroxides in organic

); mol wt 150.91. Br laBrO₃. The article of O₃, granules or cryst pow- beration of oxygen. Sol water. The aq soln is anic matter. bromide for dissolve. tassium Bromate.

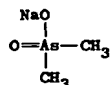
ural. BrNa; mol wt Br. Prep'd commercially sodium hydroxide soln bromate. The reaction and treated with carbon Ref: van ter Meulen, on, *Ind. Eng. Chem.* 34, lson, *Roger's Inorganic* igger, Philadelphia, 8th

ler; saline, feebly bitter t is not deliquescent. d /hat higher temp. One ut 16 ml alcohol, 6 ml y neutral. pH 6.5-8.0. om temp, sodium brom- rm of colorless crystals. avy metal salts. LD₅₀ abourger, *J. Pharmacol.*

nticonvulsant.
xen used to control con-

nethylarsino)oxy]sodium Arsecodile; Arsicodile; C₂H₄AsNaO₂; mol wt 16.82%, Na 14.37%, O nic yielding inorganic, eted partly unchanged, rep'd by the distillation otassium acetate which

yields Cadet's liquid, contg mostly dimethylarsine oxide. This is oxidized with mercuric oxide yielding crystals of cacodylic acid which is neutralized with Na₂CO₃ or NaOH: Cadet de Gassicourt, *Mem. savants étrangers* 3, 633 (1760); Valeur, Gaillot, *Compt. Rend.* 185, 956 (1927).



Trihydrate, crystals, granules. Slight odor. Liquefies in its water of hydration at about 60°. Becomes anhydr at 120°. Burns with a bluish flame, emitting a garlic-like odor. One gram dissolves in 0.5 ml water, 2.5 ml alcohol. pH about 8-9. *Keep well closed.* LD₅₀ s.c. in mice: 1.25 g/kg.

Human Toxicity: More toxic by mouth than by injection due to rapid release of inorganic arsenic by gastric acid. Large doses may cause nephritis, albuminuria, hematuria: *Martindale The Extra Pharmacopoeia*, N. W. Blacow, Ed. (Hazzell, Watson & Viney, Aylesbury, Bucks, 1972) p 219.

USE: Herbicide.

THERAP CAT: Has been used in chronic skin diseases, leukemia.

THERAP CAT (VET): Has been used in chronic eczema, anemia, as a tonic.

8340. Sodium Carbonate. CNa₂O₃; mol wt 106.00. C 11.33%, Na 43.39%, O 45.29%. Na₂CO₃. Occurs in nature as the hydrate, *thermonatrite*, and the decahydrate, *natron* or *natrite*. Produced by the ammonia-soda or Solvay process, or from lake brines or sea water by electrolytic processes: *Faith, Keyes, & Clark's Industrial Chemicals* (John Wiley, New York, 4th ed., 1975) pp 706-715. *Reviews:* Bailey in *Mellor's vol II*, suppl II, *The Alkali Metals* (part 1), 1058-1205 (1961).

Anhydr. *Solvay soda*. The technical grade (about 99% pure) is known as *soda ash*. Odorless, hygroscopic powder; alkaline taste; d 2.53; mp 851°, but begins to lose CO₂ even at 400°. On exposure to air it will gradually absorb one mol water—about 15%. Sol in 3.5 parts water at room temp, 2.2 parts water at 35°, in glycerol; insol in alcohol. Dec by acids with effervescence. Combines with water with evolution of heat. Its aq soln is strongly alkaline. pH 11.6. *Keep well closed.*

Monohydrate, odorless, small crystals or cryst powder; alkaline taste. Stable at ordinary temps and atmospheric conditions; dries out somewhat in warm, dry air or above 50°; becomes anhydr at 100°. d 2.25; also reported as 1.55. Sol in 3 parts water, 1.8 parts boiling water, 7 parts glycerol; insol in alcohol.

Decahydrate, *Nevite, Soda*. The technical product is known as *sal soda* or *washing soda*. Transparent crystals; readily effloresces on exposure to air. d 1.46. mp 34°. Sol in 2 parts cold, 0.25 part boiling water, in glycerol; insol in alcohol. The aq soln is strongly alkaline to litmus. *Keep well closed and in a cool place.*

Human Toxicity: Sensitivity reactions may occur from repeated topical use. Ingestion of large quantities may produce corrosion of G.I. tract, vomiting, diarrhea, circulatory collapse, death. Conc'd solns in contact with skin or eyes may cause local necrosis.

USE: In manuf of Na salts, glass, soap; for washing wool; textiles, etc.; in bleaching linen, cotton; general cleanser; in water-softening; in photography; as reagent in analytical chemistry.

THERAP CAT: Pharmaceutical aid (alkalizing agent).

THERAP CAT (VET): Has been used as an emetic. In solution to cleanse skin, in eczema, to soften scabs of ringworm.

8341. Sodium Carboxymethyl Cellulose. CMC; sodium cellulose glycolate; carboxymethyl cellulose sodium; Cel-O-Brandt; Cethyllose; Glykocellon; Carbose D; Thylose; Xylo-Mucine; Tylose MGA; Cellolax; Polycell. R₂OCH₂COONa. Prep'd by treating alkali cellulose with sodium chloroacetate. *Review and bibliography:* Ott, *Cellulose and Cellulose Derivatives*, New York, 1946 (2nd ed., 1955).

White granules. Soly in water depends on degree of substitution. Water-soluble CMC is available in various viscos-

ities (5-2000 centipoises in 1% soln), and the soly is equally good in hot and cold water (difference from methyl cellulose). Also the presence of metal salts has little effect on the viscosity. Solns are stable between pH 2 and 10. Below pH 2 precipitation of a solid occurs, above pH 10 the viscosity decreases rapidly. K of the free acid is 5 × 10⁻⁵. The free acid is obtained from aq soln at pH 2.5 and may be precipitated with alcohol.

USE: In drilling muds, in detergents as a soil-suspending agent, in resin emulsion paints, adhesives, printing inks, textile sizes, as protective colloid in general. In pharmacy for preparing suspensions.

THERAP CAT: Cathartic; antacid.

8342. Sodium Chlorate. ClNaO₃; mol wt 106.45. Cl 33.31%, Na 21.60%, O 45.09%. NaClO₃. The chlorate of commerce is about 99% pure. Produced from sodium chloride by electrolysis: *Faith, Keyes, & Clark's Industrial Chemicals* (John Wiley, New York, 4th ed., 1975) pp 716-721.

Colorless, odorless crystals or white granules. d 2.5. mp 248°; at about 300° liberates oxygen; entirely dec at higher temp. Sol in about 1 ml cold, 0.5 ml boiling water, about 130 ml alcohol, about 50 ml boiling alcohol, 4 ml glycerol. Sodium chloride diminishes its soly in water. The aq soln is neutral. *Keep out of contact with organic matter or other oxidizable substances.* LD orally in rats: 12,000 mg/kg. *Handbook of Toxicology vol. 1*, W. S. Spector, Ed. (Saunders, Philadelphia, 1956) pp 270-271.

USE: An oxidizer, like potassium chlorate, in manuf of dyes; explosives and matches; dyeing and printing fabrics; tanning and finishing leather; as weed killer.

THERAP CAT: Pharmaceutical aid (oxidizing agent).

8343. Sodium Chloride. Salt; common salt. ClNa; mol wt 58.45. Cl 60.66%, Na 39.34%. NaCl. The article of commerce is also known as *table salt*, *rock salt* or *sea salt*. Occurs in nature as the mineral *halite*. Produced by mining (rock salt), by evaporation of brine from underground salt deposits and from sea water by solar evaporation: *Faith, Keyes, & Clark's Industrial Chemicals* (Wiley, New York, 4th ed., 1975) pp 722-730. Comprehensive monograph: D. W. Kaufmann, *Sodium Chloride*, ACS Monograph Series no. 145 (Reinhold, New York, 1960) 743 pp.

Cubic, white crystals, granules, or powder; colorless and transparent or translucent when in large crystals. d 2.17. The salt of commerce usually contains some calcium and magnesium chlorides which absorb moisture and make it cake. mp 804° and begins to volatilize at a little above this temp. One gram dissolves in 2.8 ml water at 25°, in 2.6 ml boiling water, in 10 ml glycerol; very slightly sol in alcohol. Its soly in water is decreased by HCl and it is almost insol in conc'd HCl. Its aq soln is neutral. pH: 6.7-7.3. d of satd aq soln at 25° is 1.202. A 23% aq soln of sodium chloride freezes at -20.5°C (5°F). LD₅₀ orally in rats: 3.75 g/kg. Boyd, Shanas, *Arch. Int. Pharmacodyn. Ther.* 144, 86 (1963).

Note: *Blusalt*, a brand of sodium chloride contg trace amounts of cobalt, iodine, iron, copper, manganese, zinc is used in farm animals.

Human Toxicity: Not generally considered poisonous. Accidental substitution of NaCl for lactose in baby formulas has caused fatal poisoning.

USE: Natural salt is the source of chlorine and of sodium as well as of all, or practically all, their compds, e.g., hydrochloric acid, chlorates, sodium carbonate, hydroxide, etc.; for preserving foods; manuf soap, dyes—to salt them out; in freezing mixtures; for dyeing and printing fabrics, glazing pottery, curing hides; metallurgy of tin and other metals.

THERAP CAT: Electrolyte replenisher, emetic; topical anti-inflammatory.

THERAP CAT (VET): Essential nutrient factor. May be given orally as emetic, stomachic, laxative or to stimulate thirst (prevention of calculi). Intravenously as isotonic solution to raise blood volume, to combat dehydration. Locally as wound irrigant, rectal douche.

8344. Sodium Chlorite. ClNaO₂; mol wt 90.45. Cl 39.20%, Na 25.42%, O 35.38%. NaClO₂. Prep'd on a commercial scale by passing chlorine dioxide into a soln of sodium hydroxide contg carbonaceous matter and lime: Vincent, U.S. pats. 2,092,944/5 (1937 to Mathieson). *Review of*



ARTICLE LINKS:

Fulltext | PDF (224 K)

Sodium Picosulfate/Magnesium Citrate: A Review of its Use as a Colorectal Cleanser.

Adis Drug Evaluation

Drugs. 69(1):123-136, January 01, 2009.

Hoy, Sheridan M.; Scott, Lesley J.; Wagstaff, Antona J.

Abstract:

Oral sodium picosulfate/magnesium citrate (CitraFleet(R); Picolax(R)), consisting of sodium picosulfate (a stimulant laxative) and magnesium citrate (an osmotic laxative), is approved for use in adults (CitraFleet(R); Picolax(R)) and/or adolescents and children (Picolax(R)) as a colorectal cleansing agent prior to any diagnostic procedure (e.g. colonoscopy or x-ray examination) requiring a clean bowel and/or surgery. It is dispensed in powder form (sodium picosulfate 0.01 g, magnesium oxide 3.5 g, citric acid 12.0 g per sachet), with the magnesium oxide and citric acid components forming magnesium citrate when the powder is dissolved in water.

In adult patients, two sachets of sodium picosulfate/magnesium citrate was at least as effective and well tolerated as oral magnesium citrate 17.7 or 35.4 g, or oral polyethylene glycol 236 g in adult patients undergoing a double-contrast barium enema procedure in three large, randomized, comparative clinical studies. In contrast, sodium picosulfate/magnesium citrate was less effective than a sodium phosphate enema preparation in two studies in patients undergoing flexible sigmoidoscopy. A similar number of patients receiving two sachets of sodium picosulfate/magnesium citrate or two 45 mL doses of oral sodium phosphate the day before a double-contrast barium enema procedure achieved satisfactory barium coating and none/minimal faecal residue in one study. However, the data from three of these studies should be interpreted with caution because the administrative regimens used differed from that recommended. Sodium picosulfate/magnesium citrate is also an effective and generally well tolerated colorectal cleansing agent in children and adolescents; the preparation was more effective than oral bisacodyl 0.01 or 0.02 g plus a sodium phosphate enema preparation in this population. Further research is thus required to accurately position sodium picosulfate/magnesium citrate and fully establish its efficacy and tolerability prior to various exploratory or surgical procedures. Nevertheless, oral sodium picosulfate/magnesium citrate provides a useful option in the preparation of the colon and rectum in adults, adolescents and children undergoing any diagnostic procedure (e.g. colonoscopy or x-ray examination) requiring a clean bowel and/or surgery.

Pharmacological Properties: Oral sodium picosulfate/magnesium citrate acts locally in the colon as both a stimulant laxative, by increasing the frequency and the force of peristalsis (sodium picosulfate component), and an osmotic laxative, by retaining fluids in the colon (magnesium citrate component), to clear the colon and rectum of faecal contents. It is not absorbed in any detectable quantities. Sodium picosulfate is a prodrug: it is hydrolyzed by bacteria in the colon to the active metabolite 4,4'-dihydroxydiphenyl-(2-pyridyl)methane.

Sodium picosulfate/magnesium citrate may be associated with a dehydrating effect, as evidenced by a reduction in bodyweight and increased haemoglobin levels; some at-risk patients may experience postural hypotension and older patients may require additional electrolytes.

Clinical Efficacy: In three large (n >100), randomized, single-blind clinical studies, two sachets of oral sodium picosulfate/magnesium citrate was at least as effective as oral magnesium citrate 17.7 or 35.4 g, or oral polyethylene glycol 236 g as a colorectal cleansing agent in adult patients undergoing a double-contrast barium enema procedure. In contrast, sodium picosulfate/magnesium citrate was less effective than a sodium phosphate enema preparation in two studies in patients undergoing flexible sigmoidoscopy. A similar number of patients receiving two sachets of sodium picosulfate/magnesium citrate or two 45 mL doses of oral sodium phosphate the day before a double-contrast barium enema procedure achieved satisfactory barium coating and none/minimal faecal residue in one study. However, the data from three of these studies should be interpreted with caution because the administrative regimens used differed from that recommended.

In children and adolescents, sodium picosulfate/magnesium citrate was significantly more effective as a colorectal cleansing agent than oral bisacodyl 0.01 or 0.02 g plus a sodium phosphate enema preparation in a randomized, single-blind study; dosages were adjusted for age in this study.

Tolerability: Oral sodium picosulfate/magnesium citrate is generally well tolerated in adult patients undergoing various investigational colorectal procedures. Adverse events were generally mild to moderate in intensity and mainly gastrointestinal in nature (e.g. abdominal cramps/pain, nausea); other common treatment-emergent adverse events included disturbance of daily activity, headache and sleep disturbance. This combination is at least as well tolerated as oral sodium phosphate or oral polyethylene glycol, with moderate/severe nausea and vomiting occurring less frequently in sodium picosulfate/magnesium citrate recipients than in those receiving oral sodium phosphate, and abdominal bloating/pain and nausea developing less often with sodium picosulfate/magnesium citrate than polyethylene glycol therapy.

The incidence of abdominal pain and sleep disturbance in sodium picosulfate/magnesium citrate versus oral magnesium citrate recipients was similar in one study, but significantly lower with sodium picosulfate/magnesium citrate in another. While the incidence of most adverse events was similar in recipients of sodium picosulfate/magnesium citrate and a sodium phosphate enema preparation, more patients receiving sodium picosulfate/magnesium citrate reported moderate/severe flatulence, incontinence and sleep disturbance, and more patients receiving the enema preparation reported rectal soreness. The tolerability profile of sodium picosulfate/magnesium citrate in patients aged >70 years is reportedly similar to that in patients aged <70 years.

Abdominal pain also occurred less frequently with sodium picosulfate/magnesium citrate than with oral bisacodyl plus a sodium phosphate enema preparation in children and adolescents.

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